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(54) Title: MULTIVARIANT IL-3 HEMATOPOIESIS FUSION PROTEIN			
(57) Abstract The present invention relates to human interleukin-3 (hIL-3) variant or mutant proteins (muteins) fused with other colony stimulating factors (CSF), cytokines, lymphokines, interleukins, hematopoietic growth factors or IL-3 variants.			

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**MULTIVARIANT IL-3 HEMATOPOIESIS
FUSION PROTEIN**

This is a continuation-in-part of United States
Application Serial No. 08/192,325 filed February 04, 1994,
5 which is incorporated herein by reference.

Field of the Invention

The present invention relates to fusion molecules
10 composed of mutants or variants of human interleukin-3
(hIL-3) fused to a second colony stimulating factor (CSF)
including cytokine, lymphokine, interleukin,
hematopoietic growth factor or IL-3 variant with or
without a linker

15

Background of the Invention

Colony stimulating factors (CSFs) which stimulate
the differentiation and/or proliferation of bone marrow
cells have generated much interest because of their
20 therapeutic potential for restoring depressed levels of
hematopoietic stem cell-derived cells. CSFs in both
human and murine systems have been identified and
distinguished according to their activities. For
example, granulocyte-CSF (G-CSF) and macrophage-CSF (M-
25 CSF) stimulate the in vitro formation of neutrophilic
granulocyte and macrophage colonies, respectively while
GM-CSF and interleukin-3 (IL-3) have broader activities
and stimulate the formation of both macrophage,
neutrophilic and eosinophilic granulocyte colonies. IL-3
30 also stimulates the formation of mast, megakaryocyte and
pure and mixed erythroid colonies.

Because of its ability to stimulate the
proliferation of a number of different cell types and to
support the growth and proliferation of progenitor cells,
35 IL-3 has potential for therapeutic use in restoring
hematopoietic cells to normal amounts in those cases
where the number of cells has been reduced due to

diseases or to therapeutic treatments such as radiation and/or chemotherapy.

Interleukin-3 (IL-3) is a hematopoietic growth factor which has the property of being able to promote the survival, growth and differentiation of hematopoietic cells. Among the biological properties of IL-3 are the ability (a) to support the growth and differentiation of progenitor cells committed to all, or virtually all, blood cell lineages; (b) to interact with early multipotential stem cells; (c) to sustain the growth of pluripotent precursor cells; (d) to stimulate proliferation of chronic myelogenous leukemia (CML) cells; (e) to stimulate proliferation of mast cells, eosinophils and basophils; (f) to stimulate DNA synthesis by human acute myelogenous leukemia (AML) cells; (g) to prime cells for production of leukotrienes and histamines; (h) to induce leukocyte chemotaxis; and (i) to induce cell surface molecules needed for leukocyte adhesion.

Mature human interleukin-3 (hIL-3) consists of 133 amino acids. It has one disulfide bridge and two potential glycosylation sites (Yang, et al., CELL 47:3 (1986)).

Murine IL-3 (mIL-3) was first identified by Ihle, et al., J. IMMUNOL. 126:2184 (1981) as a factor which induced expression of a T cell associated enzyme, 20 - hydroxysteroid dehydrogenase. The factor was purified to homogeneity and shown to regulate the growth and differentiation of numerous subclasses of early hematopoietic and lymphoid progenitor cells.

In 1984, cDNA clones coding for murine IL-3 were isolated (Fung, et al., NATURE 307:233 (1984) and Yokota, et al., PROC. NATL. ACAD. SCI. USA 81:1070 (1984)). The murine DNA sequence coded for a polypeptide of 166 amino acids including a putative signal peptide.

The gibbon IL-3 sequence was obtained using a gibbon cDNA expression library. The gibbon IL-3 sequence was

then used as a probe against a human genomic library to obtain a human IL-3 sequence.

Gibbon and human genomic DNA homologues of the murine IL-3 sequence were disclosed by Yang, et al., CELL 47:3 (1986). The human sequence reported by Yang, et al. included a serine residue at position 8 of the mature protein sequence. Following this finding, others reported isolation of Pro⁸ hIL-3 cDNAs having proline at position 8 of the protein sequence. Thus it appears that there may be two allelic forms of hIL-3.

Dorssers, et al., GENE 55:115 (1987), found a clone from a human cDNA library which hybridized with mIL-3. This hybridization was the result of the high degree of homology between the 3' noncoding regions of mIL-3 and hIL-3. This cDNA coded for an hIL-3 (Pro⁸) sequence.

U.S. 4,877,729 and U.S. 4,959,454 disclose human IL-3 and gibbon IL-3 cDNAs and the protein sequences for which they code. The hIL-3 disclosed has serine rather than proline at position 8 in the protein sequence.

Clark-Lewis, et al., SCIENCE 231:134 (1986) performed a functional analysis of murine IL-3 analogs synthesized with an automated peptide synthesizer. The authors concluded that the stable tertiary structure of the complete molecule was required for full activity. A study on the role of the disulfide bridges showed that replacement of all four cysteines by alanine gave a molecule with 1/500th the activity as the native molecule. Replacement of two of the four Cys residues by Ala(Cys⁷⁹, Cys¹⁴⁰ -> Ala⁷⁹, Ala¹⁴⁰) resulted in an increased activity. The authors concluded that in murine IL-3 a single disulfide bridge is required between cysteines 17 and 80 to get biological activity that approximates physiological levels and that this structure probably stabilizes the tertiary structure of the protein to give a conformation that is optimal for function. (Clark-Lewis, et al., PROC. NATL. ACAD. SCI. USA 85:7897 (1988)).

International Patent Application (PCT) WO 88/00598 discloses gibbon- and human-like IL-3. The hIL-3 contains a Ser⁸ -> Pro⁸ replacement. Suggestions are made to replace Cys by Ser, thereby breaking the
5 disulfide bridge, and to replace one or more amino acids at the glycosylation sites.

EP-A-0275598 (WO 88/04691) illustrates that Ala¹ can be deleted while retaining biological activity. Some mutant hIL-3 sequences are provided, e.g., two double
10 mutants, Ala¹ -> Asp¹, Trp¹³ -> Arg¹³ (pGB/IL-302) and Ala¹ -> Asp¹, Met³ -> Thr³ (pGB/IL-304) and one triple mutant Ala¹ -> Asp¹, Leu⁹ -> Pro⁹, Trp¹³ -> Arg¹³ (pGB/IL-303).

WO 88/05469 describes how deglycosylation mutants
15 can be obtained and suggests mutants of Arg⁵⁴Arg⁵⁵ and Arg¹⁰⁸Arg¹⁰⁹Lys¹¹⁰ might avoid proteolysis upon expression in Saccharomyces cerevisiae by KEX2 protease. No mutated proteins are disclosed. Glycosylation and the KEX2 protease activity are only important, in this
20 context, upon expression in yeast.

WO 88/06161 mentions various mutants which theoretically may be conformationally and antigenically neutral. The only actually performed mutations are Met² -> Ile² and Ile¹³¹ -> Leu¹³¹. It is not disclosed
25 whether the contemplated neutralities were obtained for these two mutations.

WO 91/00350 discloses nonglycosylated hIL-3 analog proteins, for example, hIL-3 (Pro⁸Asp¹⁵Asp⁷⁰), Met³ rhuIL-3 (Pro⁸Asp¹⁵Asp⁷⁰); Thr⁴ rhuIL-3
30 (Pro⁸Asp¹⁵Asp⁷⁰) and Thr⁶ rhuIL-3 (Pro⁸Asp¹⁵Asp⁷⁰). It is said that these protein compositions do not exhibit certain adverse side effects associated with native hIL-3 such as urticaria resulting from infiltration of mast cells and lymphocytes into the dermis. The disclosed
35 analog hIL-3 proteins may have N termini at Met³, Thr⁴, or Thr⁶.

WO 91/12874 discloses cysteine added variants (CAVs)

of IL-3 which have at least one Cys residue substituted for a naturally occurring amino acid residue.

U.S. 4,810,643 discloses the DNA sequence encoding human G-CSF.

5 WO 91/02754 discloses a fusion protein composed of GM-CSF and IL-3 which has increased biological activity compared to GM-CSF or IL-3 alone. Also disclosed are nonglycosylated IL-3 and GM-CSF analog proteins as components of the fusion.

10 WO 92/04455 discloses fusion proteins composed of IL-3 fused to a lymphokine selected from the group consisting of IL-3, IL-6, IL-7, IL-9, IL-11, EPO and G-CSF.

15

Summary of the Invention

The present invention encompasses recombinant human interleukin-3 (hIL-3) variant or mutant proteins (muteins) fused to a second colony stimulating factor (CSF) include, cytokine, lymphokine, interleukin, 20 hematopoietic growth factor (herein collectively referred to as "colony stimulating factors") or IL-3 variant with or without a linker. These hIL-3 muteins contain amino acid substitutions and may also have amino acid deletions at either/or both the N- and C- termini. This invention 25 encompasses mixed function colony stimulating factors formed from covalently linked polypeptides, each of which may act through a different and specific cell receptor to initiate complementary biological activities.

Novel compounds of this invention are represented by 30 the formulas

35 R1-L-R2, R2-L-R1, R1-R2, R2-R1, R1-L-R1 and R1-R1 where R1 is a hIL-3 variant which contains multiple amino acid substitutions and which may have portions of the hIL-3 molecule deleted, R2 is an IL-3, IL-3 variant or CSF with a different but complementary activity. The R1 polypeptide is fused either directly or through a linker segment to the R2 polypeptide. Thus L represents a

chemical bond or polypeptide segment to which both R1 and R2 are fused. Preferably, these mutant IL-3 polypeptides of the present invention contain four or more amino acids which differ from the amino acids found at the
5 corresponding positions in the native hIL-3 polypeptide. The invention also relates to pharmaceutical compositions containing the fusion molecules, DNA coding for the fusion molecules, and methods for using the fusion
10 molecules. Additionally, the present invention relates to recombinant expression vectors comprising nucleotide sequences encoding the hIL-3 fusion molecules, related microbial expression systems, and processes for making the fusion molecules using the microbial expression systems.

15 These fusion molecules may be characterized by having the usual activity of both of the peptides forming the fusion molecule or it may be further characterized by having a biological or physiological activity greater than simply the additive function of the presence of IL-3
20 or the second colony stimulating factor alone. The fusion molecule may also unexpectedly provide an enhanced effect on the activity or an activity different from that expected by the presence of IL-3 or the second colony stimulating factor or IL-3 variant. The fusion molecule
25 may also have an improved activity profile which may include reduction of undesirable biological activities associated with native hIL-3.

The present invention also includes mutants of hIL-3 in which from 1 to 14 amino acids have been deleted from
30 the N-terminus and/or from 1 to 15 amino acids have been deleted from the C-terminus, containing multiple amino acid substitutions, to which a second colony stimulating factor or IL-3 variant has been fused. Preferred fusion molecules of the present invention are composed of hIL-3
35 variants in which amino acids 1 to 14 have been deleted from the N-terminus, amino acids 126 to 133 have been deleted from the C-terminus, and contains from about four

to about twenty-six amino acid substitutions in the polypeptide sequence fused to second colony stimulating factor or IL-3 variant.

The present invention also provides fusion molecules which may function as IL-3 antagonists or as discrete antigenic fragments for the production of antibodies useful in immunoassay and immunotherapy protocols.

Antagonists of hIL-3 would be particularly useful in blocking the growth of certain cancer cells like AML, CML and certain types of B lymphoid cancers. Other conditions where antagonists would be useful include those in which certain blood cells are produced at abnormally high numbers or are being activated by endogenous ligands. Antagonists would effectively compete for ligands, presumably naturally occurring hemopoietins including and not limited to IL-3, GM-CSF and IL-5, which might trigger or augment the growth of cancer cells by virtue of their ability to bind to the IL-3 receptor complex while intrinsic activation properties of the ligand are diminished. IL-3, GM-CSF and/or IL-5 also play a role in certain asthmatic responses. An antagonist of the IL-3 receptor may have the utility in this disease by blocking receptor-mediated activation and recruitment of inflammatory cells.

In addition to the use of the fusion molecules of the present invention in vivo, it is envisioned that in vitro uses would include the ability to stimulate bone marrow and blood cell activation and growth before infusion into patients.

Brief Description of the Drawings

Figure 1 is the human IL-3 gene for E. coli expression (pMON5873), encoding the polypeptide sequence of natural (wild type) human IL-3 [SEQ ID NO:49], plus an initiator methionine, as expressed in E. coli, with the amino acids numbered from the N-terminus of the natural hIL-3.

Figure 2 is the construction of plasmids pMON13018 and pMON13021. The plasmid pMON13018 is an intermediate plasmid used to construct the plasmid pMON13021 which encodes the polypeptide fusion pMON13021.

5 Figure 3 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusion pMON3988.

Figure 4 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusions
10 pMON3987 and pMON26430, pMON3995 and pMON26415.

Figure 5 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusion pMON26425.

Figure 6 is the bioactivity, as measured in the
15 methylcellulose assay, of the polypeptide fusions pMON26406 and pMON26433.

Figure 7 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusions
20 pMON26431 and pMON26427.

Detailed Description of the Invention

The present invention encompasses recombinant human interleukin-3 (hIL-3) variants or mutant proteins
25 (muteins) fused to itself, IL-3 or a second colony-stimulating factor (CSF) including but not limited to cytokine, lymphokine, interleukin, hematopoietic growth factor or IL-3 variant with or without a linker. This invention encompasses mixed function colony stimulating
30 factors formed from covalently linked polypeptides, each of which may act through a different and specific cell receptor to initiate complementary biological activities. Hematopoiesis requires a complex series of cellular events in which stem cells generate continuously into
35 large populations of maturing cells in all major lineages. There are currently at least 20 known regulators with hematopoietic proliferative activity.

Most of these proliferative regulators can stimulate one or another type of colony formation in vitro, the precise pattern of colony formation stimulated by each regulator is quite distinctive. No two regulators stimulate exactly the same pattern of colony formation, as evaluated by colony numbers or, more importantly, by the lineage and maturation pattern of the cells making up the developing colonies. Proliferative responses can most readily be analyzed in simplified in vitro culture systems. Three quite different parameters can be distinguished: alteration in colony size, alteration in colony numbers and cell lineage. Two or more factors may act on the progenitor cell, inducing the formation of larger number of progeny thereby increasing the colony size. Two or more factors may allow increased number of progenitor cells to proliferate either because distinct subsets of progenitors cells exist that respond exclusively to one factor or because some progenitors require stimulation by two or more factors before being able to respond. Activation of additional receptors on a cell by the use of two or more factors is likely to enhance the mitotic signal because of coalescence of initially differing signal pathways into a common final pathway reaching the nucleus (Metcalf, 1989). Other mechanisms could explain synergy. For example, if one signaling pathway is limited by an intermediate activation of an additional signaling pathway by a second factor may result in a superadditive response. In some cases, activation of one receptor type can induce a enhanced expression of other receptors (Metcalf, 1993). Two or more factors may result in a different pattern of cell lineages then from a single factor. The use of fusion molecules may have the potential clinical advantage resulting from a proliferative response that is not possible by any single factor.

Hematopoietic and other growth factors can be grouped in to two distinct families of related receptors:

(1) tyrosine kinase receptors, including those for epidermal growth factor, M-CSF (Sherr, 1990) and SCF (Yarden et al., 1987); and (2) hematopoietic receptors, not containing a tyrosine kinase domain, but exhibiting obvious homology in their extracellular domain (Bazan, 1990). Included in this later group are erythropoietin (EPO) (D'Andrea et al., 1989), GM-CSF (Gearing et al., 1989), IL-3 (Kitamura et al., 1991), G-CSF (Fukunaga et al., 1990), IL-4 (Harada et al., 1990), IL-5 (Takaki et al., 1990), IL-6 (Yamasaki et al., 1988), IL-7 (Goodwin et al., 1990), LIF (Gearing et al., 1991) and IL-2 (Cosman et al., 1987). Most of the later group of receptors exists in high-affinity form as a heterodimers. After ligand binding, the specific α -chains become associated with at least one other receptor chain (β -chain, γ -chain). Many of these factors share a common receptor subunit. The α -chains for GM-CSF, IL-3 and IL-5 share the same β -chain (Kitamura et al., 1991; Takaki et al., 1991) and receptor complexes for IL-6, LIF and IL-11 share a common β -chain (gp130) (Taga et al., 1989; Gearing et al., 1992). The receptor complexes of IL-2, IL-4 and IL-7 share a common γ -chain (Kondo et al., 1993; Russell et al., 1993; Noguchi et al., 1993).

The use of multiple factors may also have potential advantage by lowering the demands placed on factor-producing cells and their induction systems. If there are limitations in the ability of a cell to produce a factor then by lowering the required concentrations of each of the factors by using them in combination may usefully reduce demands on the factor-producing cells. The use of multiple factors may lower the amount of the factors that would be needed, probably reducing the likelihood of adverse responses.

Novel compounds of this invention are represented by a formula selected from the group consisting of

R1-L-R2, R2-L-R1, R1-R2, R2-R1, R1-L-R1 and R1-R1

where R1 is a hIL-3 variant which contains multiple amino acid substitutions and which may have portions of the hIL-3 molecule deleted as is disclosed in co-pending United States Patent Application Serial number PCT/US93/11197, R2 is IL-3, IL-3 variant or a colony stimulating factor with a different but complementary activity. By complementary activity is meant activity which enhances or changes the response to another cell modulator. The R1 polypeptide is fused either directly or through a linker segment to the R2 polypeptide. The term "directly" defines fusions in which the polypeptides are joined without a peptide linker. Thus L represents a chemical bound or polypeptide segment to which both R1 and R2 are fused in frame, most commonly L is a linear peptide to which R1 and R2 are bound by amide bonds linking the carboxy terminus of R1 to the amino terminus of L and carboxy terminus of L to the amino terminus of R2. By "fused in frame" is meant that there is no translation termination or disruption between the reading frames of R1 and R2. A nonexclusive list of other growth factors, colony stimulating factors (CSFs), cytokine, lymphokine, interleukin, hematopoietic growth factor within the definition of R2, which can be fused to a hIL-3 variant of the present invention include GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF) also known as steel factor or c-kit ligand. Additionally, this invention encompasses the use of modified R2 molecules or mutated or modified DNA sequences encoding these R2 molecules. The present invention also includes fusion molecules in which R2 is a hIL-3 variant which means an IL-3 in which has amino acid substitutions and which may have portions of the hIL-3 molecule deleted such as what

is disclosed in PCT/US93/11197 and PCT/US93/11198 as well as other variants known in the art.

The linking group (L) is generally a polypeptide of between 1 and 500 amino acids in length. The linkers joining the two molecules are preferably designed to (1) allow the two molecules to fold and act independently of each other, (2) not have a propensity for developing an ordered secondary structure which could interfere with the functional domains of the two proteins, (3) have minimal hydrophobic or charged characteristic which could interact with the functional protein domains and (4) provide steric separation of R1 and R2 such that R1 and R2 could interact simultaneously with their corresponding receptors on a single cell. Typically surface amino acids in flexible protein regions include Gly, Asn and Ser. Virtually any permutation of amino acid sequences containing Gly, Asn and Ser would be expected to satisfy the above criteria for a linker sequence. Other neutral amino acids, such as Thr and Ala, may also be used in the linker sequence. Additional amino acids may also be included in the linkers due to the addition of unique restriction sites in the linker sequence to facilitate construction of the fusions.

Preferred linkers of the present invention include sequences selected from the group of formulas:
(Gly₃Ser)_n, (Gly₄Ser)_n, (Gly₅Ser)_n, (Gly_nSer)_n or (AlaGlySer)_n

One example of a highly-flexible linker is the (GlySer)-rich spacer region present within the pIII protein of the filamentous bacteriophages, e.g. bacteriophages M13 or fd (Schaller et al., 1975). This region provides a long, flexible spacer region between two domains of the pIII surface protein. The spacer region consists of the amino acid sequence:
GlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGluGlyGlyGlySerGluGlyGlySerGluGlyGlyGlySerGlyGlyGlySer
[SEQ ID NO:50]

The present invention also includes linkers in which an endopeptidase recognition sequence is included. Such a cleavage site may be valuable to separate the individual components of the fusion to determine if they are properly folded and active in vitro. Examples of various endopeptidases include, but are not limited to, Plasmin, Enterokinase, Kallikrein, Urokinase, Tissue Plasminogen activator, clostripain, Chymosin, Collagenase, Russell's Viper Venom Protease, Postproline cleavage enzyme, V8 protease, Thrombin and factor Xa.

Peptide linker segments from the hinge region of heavy chain immunoglobulins IgG, IgA, IgM, IgD or IgE provide an angular relationship between the attached polypeptides. Especially useful are those hinge regions where the cysteines are replaced with serines. Preferred linkers of the present invention include sequences derived from murine IgG gamma 2b hinge region in which the cysteines have been changed to serines. These linkers may also include an endopeptidase cleavage site. Examples of such linkers include the following sequences selected from the group of sequences

IleSerGluProSerGlyProIleSerThrIleAsnProSerProProSerLys
GluSerHisLysSerPro [SEQ ID NO:51]

IleGluGlyArgIleSerGluProSerGlyProIleSerThrIleAsnProSer
ProProSerLysGluSerHisLysSerPro [SEQ ID NO:52]

The present invention is, however, not limited by the form, size or number of linker sequences employed and the only requirement of the linker is that functionally it does not interfere adversely with the folding and function of the individual molecules of the fusion.

An alternative method for connecting two hematopoietic growth factors is by means of a non-covalent interaction. Such complexed proteins can be described by one the formulae:

R1-C1 + R2-C2; or C1-R1 + C2-R2; C1-R1 + R2-C2; or C1-R1 + R2-C2.

5 where R1 is a hIL-3 variant which contains multiple amino acid substitutions and which may have portions of the hIL-3 molecule deleted, R2 is a colony stimulating factor with a different but complementary activity. A nonexclusive list of other growth hormones, colony
10 stimulating factors (CSFs), cytokine, lymphokine, interleukin, hematopoietic growth factor within the definition of R2, which can be fused to a hIL-3 variant of the present invention include GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-
15 CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF) also known as steel
20 factor or c-kit ligand. Domains C1 and C2 are either identical or non-identical chemical structures, typically proteinaceous, which can form a non-covalent, specific association. Complexes between C1 and C2 result in a one-to-one stoichiometric relationship between R1 and R2
25 for each complex. Examples of domains which associate are "leucine zipper" domains of transcription factors, dimerization domains of bacterial transcription repressors and immunoglobulin constant domains. Covalent bonds link R1 and C1, and R2 and C2, respectively. As
30 indicated in the formulae, the domains C1 and C2 can be present either at the N-terminus or C-terminus of their corresponding hematopoietic growth factor (R). These multimerization domains (C1 and C2) include those derived from the bZIP family of proteins (Abel et al., 1989; Landshulz et al., 1988; Pu et al., 1993; Kozarides et al., 1988) as well as multimerization domains of the helix-loop-helix family of proteins (Abel et al., 1989;

Murre et al., 1989; Tapscott et al., 1988; Fisher et al., 1991). Preferred fusions of the present invention include colony stimulating factors dimerized by virtue of their incorporation as translational fusions the leucine zipper dimerization domains of the bZIP family proteins Fos and Jun. The leucine zipper domain of Jun is capable of interacting with identical domains. On the other hand, the leucine zipper domain of Fos interacts with the Jun leucine zipper domain, but does not interact with other Fos leucine zipper domains. Mixtures of Fos and Jun predominantly result in formation of Fos-Jun heterodimers. Consequently, when fused to colony stimulating factors, the Jun domain can be used to direct the formation of either homo or heterodimers.

15 Preferential formation of heterodimers can be achieved if one of the colony stimulating factor partner is engineered to possess the Jun leucine zipper domain while the other is engineered to possess the Fos zipper.

Peptides may also be added to facilitate purification or identification of fusion proteins (e.g., poly-His). A highly antigenic peptide may also be added that would enable rapid assay and facile purification of the fusion protein by a specific monoclonal antibody.

The present invention relates to novel fusion molecules composed of novel variants of human interleukin-3 (hIL-3) in which amino acid substitutions have been made at four or more positions in amino acid sequence of the polypeptide fused to second colony stimulating factor or IL-3 variant. Preferred fusion molecules of the present invention are (15-125)hIL-3 deletion mutants which have deletions of amino acids 1 to 14 at the N-terminus and 126 to 133 at the C-terminus and which also have four or more amino acid substitutions in the polypeptide fused to second colony stimulating factor or IL-3 variant. The present invention includes mutant polypeptides comprising minimally amino acids residues 15 to 118 of hIL-3 with or without additional amino acid

extensions to the N-terminus and/or C-terminus which further contain four or more amino acid substitutions in the amino acid sequence of the polypeptide fused to another colony stimulating factor or IL-3 variant.

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As used herein human interleukin-3 corresponds to the amino acid sequence (1-133) as depicted in Figure 1 and (15-125) hIL-3 corresponds to the 15 to 125 amino acid sequence of the hIL-3 polypeptide. Naturally occurring variants of hIL-3 polypeptide amino acids are also included in the present invention (for example, the allele in which proline rather than serine is at position 8 in the hIL-3 polypeptide sequence) as are variant hIL-3 molecules which are modified post-translationally (e.g. glycosylation).

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"Mutant amino acid sequence," "mutant protein" or "mutant polypeptide" refers to a polypeptide having an amino acid sequence which varies from a native sequence or is encoded by a nucleotide sequence intentionally made variant from a native sequence. "Mutant protein," "variant protein" or "mutein" means a protein comprising a mutant amino acid sequence and includes polypeptides which differ from the amino acid sequence of native hIL-3 due to amino acid deletions, substitutions, or both. "Native sequence" refers to an amino acid or nucleic acid sequence which is identical to a wild-type or native form of a gene or protein.

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Human IL-3 can be characterized by its ability to stimulate colony formation by human hematopoietic progenitor cells. The colonies formed include erythroid, granulocyte, megakaryocyte, granulocytic macrophages and mixtures thereof. Human IL-3 has demonstrated an ability to restore bone marrow function and peripheral blood cell populations to therapeutically beneficial levels in studies performed initially in primates and subsequently in humans (Gillio, A. P., et al. (1990); Ganser, A, et

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al. (1990); Falk, S., et al. (1991). Additional activities of hIL-3 include the ability to stimulate leukocyte migration and chemotaxis; the ability to prime human leukocytes to produce high levels of inflammatory mediators like leukotrienes and histamine; the ability to induce cell surface expression of molecules needed for leukocyte adhesion; and the ability to trigger dermal inflammatory responses and fever. Many or all of these biological activities of hIL-3 involve signal transduction and high affinity receptor binding. Fusion molecules of the present invention may exhibit useful properties such as having similar or greater biological activity when compared to native hIL-3 or by having improved half-life or decreased adverse side effects, or a combination of these properties. They may also be useful as antagonists. Fusion molecules which have little or no activity when compared to native hIL-3 may still be useful as antagonists, as antigens for the production of antibodies for use in immunology or immunotherapy, as genetic probes or as intermediates used to construct other useful hIL-3 muteins.

The novel fusion molecules of the present invention will preferably have at least one biological property of human IL-3 and the other colony stimulating factor or IL-3 variant to which it is fused and may have more than one IL-3-like biological property, or an improved property, or a reduction in an undesirable biological property of human IL-3. Some mutant polypeptides of the present invention may also exhibit an improved side effect profile. For example, they may exhibit a decrease in leukotriene release or histamine release when compared to native hIL-3 or (15-125) hIL-3. Such hIL-3 or hIL-3-like biological properties may include one or more of the following biological characteristics and in vivo and in vitro activities.

One such property is the support of the growth and differentiation of progenitor cells committed to

erythroid, lymphoid, and myeloid lineages. For example, in a standard human bone marrow assay, an IL-3-like biological property is the stimulation of granulocytic type colonies, megakaryocytic type colonies, monocyte/macrophage type colonies, and erythroid bursts. Other IL-3-like properties are the interaction with early multipotential stem cells, the sustaining of the growth of pluripotent precursor cells, the ability to stimulate chronic myelogenous leukemia (CML) cell proliferation, the stimulation of proliferation of mast cells, the ability to support the growth of various factor-dependent cell lines, and the ability to trigger immature bone marrow cell progenitors. Other biological properties of IL-3 have been disclosed in the art. Human IL-3 also has some biological activities which may in some cases be undesirable, for example the ability to stimulate leukotriene release and the ability to stimulate increased histamine synthesis in spleen and bone marrow cultures and in vivo.

Biological activity of hIL-3 and hIL-3 fusion proteins of the present invention is determined by DNA synthesis by human acute myelogenous leukemia cells (AML). The factor-dependent cell line AML 193 was adapted for use in testing biological activity. The biological activity of hIL-3 and hIL-3 fusion proteins of the present invention is also determined by counting the colony forming units in a bone marrow assay.

Other in vitro cell based assays may also be useful to determine the activity of the fusion molecules depending on the colony stimulating factors that comprise the fusion. The following are examples of other useful assays.

TF-1 proliferation assay: The TF-1 cell line was derived from bone marrow of a patient with erythroleukemia (Kitamura et al., 1989). TF-1 cells respond to IL-3, GM-CSF, EPO and IL-5.

32D proliferation assay: 32D is a murine IL-3 dependent cell line which does not respond to human IL-3 but does respond to human G-CSF which is not species restricted.

T1165 proliferation assay: T1165 cells are a IL-6 dependent murine cell line (Nordan et al., 1986) which respond to IL-6 and IL-11.

Human Plasma Clot meg-CSF Assay: Used to assay megakaryocyte colony formation activity (Mazur et al., 1981).

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One object of the present invention is to provide hIL-3 variant with four or more amino acid substitutions in the polypeptide sequence fused to a second colony stimulating factor or IL-3 variant, which have similar or improved biological activity in relation to native hIL-3 or the second colony stimulating factor or IL-3 variant.

The hIL-3 variant fusion molecules of the present invention may have hIL-3 or hIL-3-like activity. For example, they may possess one or more of the biological activities of native hIL-3 and may be useful in stimulating the production of hematopoietic cells by human or primate progenitor cells. The fusion molecules of the present invention and pharmaceutical compositions containing them may be useful in the treatment of conditions in which hematopoietic cell populations have been reduced or destroyed due to disease or to treatments such as radiation or chemotherapy. Pharmaceutical compositions containing fusion molecules of the present invention can be administered parenterally, intravenously, or subcutaneously.

Native hIL-3 possesses considerable inflammatory activity and has been shown to stimulate synthesis of the arachidonic acid metabolites LTC₄, LTD₄, and LTE₄; histamine synthesis and histamine release. Human clinical trials with native hIL-3 have documented inflammatory responses (Biesma, et al., BLOOD, 80:1141-1148 (1992) and Postmus, et al., J. CLIN. ONCOL.,

10:1131-1140 (1992)). A recent study indicates that leukotrienes are involved in IL-3 actions in vivo and may contribute significantly to the biological effects of IL-3 treatment (Denzlinger, C., et al., BLOOD, 81:2466-2470 (1993))

5 Some fusion molecules of the present invention may have an improved therapeutic profile as compared to native hIL-3. For example, some fusion molecules of the present invention may have a similar or more potent
10 growth factor activity relative to native hIL-3 without having a similar or corresponding increase in the stimulation of leukotriene or histamine. These fusion molecules would be expected to have a more favorable therapeutic profile since the amount of polypeptide which
15 needs to be given to achieve the desired growth factor activity (e. g. cell proliferation) would have a lesser leukotriene or histamine stimulating effect. In studies with native hIL-3, the stimulation of inflammatory factors has been an undesirable side effect of the
20 treatment. Reduction or elimination of the stimulation of mediators of inflammation would provide an advantage over the use of native hIL-3.

Novel fusion molecules of the present invention may also be useful as antagonists which block the hIL-3
25 receptor by binding specifically to it and preventing binding of the agonist.

One potential advantage of the novel fusion
molecules of the present invention, particularly those which retain activity similar to or better than that of
30 native hIL-3, is that it may be possible to use a smaller amount of the biologically active mutein to produce the desired therapeutic effect. This may make it possible to reduce the number of treatments necessary to produce the desired therapeutic effect. The use of smaller amounts
35 may also reduce the possibility of any potential antigenic effects or other possible undesirable side effects. For example, if a desired therapeutic effect

can be achieved with a smaller amount of polypeptide it may be possible to reduce or eliminate side effects associated with the administration of native IL-3 such as the stimulation of leukotriene and/or histamine release.

5 The novel fusion molecules of the present invention may also be useful in the activation of stem cells or progenitors which have low receptor numbers.

The present invention also includes the DNA sequences which code for the fusion proteins, DNA sequences which are substantially similar and perform substantially the same function, and DNA sequences which differ from the DNAs encoding the fusion molecules of the invention only due to the degeneracy of the genetic code. Also included in the present invention are; the

15 oligonucleotide intermediates used to construct the mutant DNAs; and the polypeptides coded for by these oligonucleotides. These polypeptides may be useful as antagonists or as antigenic fragments for the production of antibodies useful in immunoassay and immunotherapy protocols.

Compounds of this invention are preferably made by genetic engineering techniques now standard in the art United States Patent 4,935,233 and Sambrook et al., "Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory (1989)]. One method of creating the preferred hIL-3 (15-125) mutant genes is cassette mutagenesis [Wells, et al. (1985)] in which a portion of the coding sequence of hIL-3 in a plasmid is replaced with synthetic oligonucleotides that encode the desired

30 amino acid substitutions in a portion of the gene between two restriction sites. In a similar manner amino acid substitutions could be made in the full-length hIL-3 gene, or genes encoding variants of hIL-3 in which from 1 to 14 amino acids have been deleted from the N-terminus and/or from 1 to 15 amino acids have been deleted from

35 the C-terminus. When properly assembled these oligonucleotides would encode hIL-3 variants with the

desired amino acid substitutions and/or deletions from the N-terminus and/or C-terminus. These and other mutations could be created by those skilled in the art by other mutagenesis methods including; oligonucleotide-directed mutagenesis [Zoller and Smith (1982, 1983, 1984), Smith (1985), Kunkel (1985), Taylor, et al. (1985), Deng and Nickoloff (1992)] or polymerase chain reaction (PCR) techniques [Saiki, (1985)].

Pairs of complementary synthetic oligonucleotides encoding the desired gene can be made and annealed to each other. The DNA sequence of the oligonucleotide would encode sequence for amino acids of desired gene with the exception of those substituted and/or deleted from the sequence.

Plasmid DNA can be treated with the chosen restriction endonucleases then ligated to the annealed oligonucleotides. The ligated mixtures can be used to transform competent JM101 cells to resistance to an appropriate antibiotic. Single colonies can be picked and the plasmid DNA examined by restriction analysis and/or DNA sequencing to identify plasmids with the desired genes.

Fusing of the DNA sequences of the hIL-3 variant with the DNA sequence of the other colony stimulating factor or IL-3 variant may be accomplished by the use of intermediate vectors. Alternatively one gene can be cloned directly into a vector containing the other gene. Linkers and adapters can be used for joining the DNA sequences, as well as replacing lost sequences, where a restriction site was internal to the region of interest. Thus genetic material (DNA) encoding one polypeptide, peptide linker, and the other polypeptide is inserted into a suitable expression vector which is used to transform bacteria, yeast, insect cell or mammalian cells. The transformed organism is grown and the protein isolated by standard techniques. The resulting product is therefore a new protein which has a hIL-3 variant joined

by a linker region to a second colony stimulating factor or IL-3 variant.

Another aspect of the present invention provides plasmid DNA vectors for use in the expression of these novel fusion molecules. These vectors contain the novel DNA sequences described above which code for the novel polypeptides of the invention. Appropriate vectors which can transform microorganisms capable of expressing the fusion molecules include expression vectors comprising nucleotide sequences coding for the fusion molecules joined to transcriptional and translational regulatory sequences which are selected according to the host cells used.

Vectors incorporating modified sequences as described above are included in the present invention and are useful in the production of the fusion polypeptides. The vector employed in the method also contains selected regulatory sequences in operative association with the DNA coding sequences of the invention and capable of directing the replication and expression thereof in selected host cells.

As another aspect of the present invention, there is provided a method for producing the novel fusion molecules. The method of the present invention involves culturing a suitable cell or cell line, which has been transformed with a vector containing a DNA sequence coding for expression of a novel hIL-3 variant fusion molecule. Suitable cells or cell lines may be bacterial cells. For example, the various strains of E. coli are well-known as host cells in the field of biotechnology. Examples of such strains include E. coli strains JM101 [Yanish-Perron, et al. (1985)] and MON105 [Obukowicz, et al. (1992)]. Also included in the present invention is the expression of the fusion protein utilizing a chromosomal expression vector for E. coli based on the bacteriophage Mu (Weinberg et al., 1993). Various strains of B. subtilis may also be employed in this

method. Many strains of yeast cells known to those skilled in the art are also available as host cells for expression of the polypeptides of the present invention. When expressed in the E. coli cytoplasm, the above-mentioned mutant hIL-3 variant fusion molecules of the present invention may also be constructed with Met-Ala- at the N-terminus so that upon expression the Met is cleaved off leaving Ala at the N-terminus. The fusion molecules of the present invention may include fusion polypeptides having Met-, Ala- or Met-Ala- attached to the N-terminus. When the fusion molecules are expressed in the cytoplasm of E. coli, polypeptides with and without Met attached to the N-terminus are obtained. The N-termini of proteins made in the cytoplasm of E. coli are affected by posttranslational processing by methionine aminopeptidase (Ben-Bassat et al., 1987) and possibly by other peptidases. These mutant fusion molecules may also be expressed in E. coli by fusing a signal peptide to the N-terminus. This signal peptide is cleaved from the polypeptide as part of the secretion process. Secretion in E. coli can be used to obtain the correct amino acid at the N-terminus (e.g., Asn¹⁵ in the (15-125) hIL-3 polypeptide) due to the precise nature of the signal peptidase. This is in contrast to the heterogeneity often observed at the N-terminus of proteins expressed in the cytoplasm in E. coli.

Also suitable for use in the present invention are mammalian cells, such as Chinese hamster ovary cells (CHO). General methods for expression of foreign genes in mammalian cells are reviewed in: Kaufman, R. J. (1987) High level production of proteins in mammalian cells, in Genetic Engineering, Principles and Methods, Vol. 9, J. K. Setlow, editor, Plenum Press, New York. An expression vector is constructed in which a strong promoter capable of functioning in mammalian cells drives transcription of a eukaryotic secretion signal peptide coding region, which is translationally fused to the coding region for

the fusion molecule. For example, plasmids such as pcDNA I/Neo, pRC.RSV, and pRC.CMV (obtained from Invitrogen Corp., San Diego, California) can be used. The eukaryotic secretion signal peptide coding region can be from the hIL-3 gene itself or it can be from another secreted mammalian protein (Bayne, M. L. et al. (1987) Proc. Natl. Acad. Sci. USA 84, 2638-2642). After construction of the vector containing the hIL-3 variant gene, the vector DNA is transfected into mammalian cells. Such cells can be, for example, the COS7, HeLa, BHK, CHO, or mouse L lines. The cells can be cultured, for example, in DMEM media (JRH Scientific). The hIL-3 variant secreted into the media can be recovered by standard biochemical approaches following transient expression 24 - 72 hours after transfection of the cells or after establishment of stable cell lines following selection for neomycin resistance. The selection of suitable mammalian host cells and methods for transformation, culture, amplification, screening and product production and purification are known in the art. See, e.g., Gething and Sambrook, Nature, 293:620-625 (1981), or alternatively, Kaufman et al, Mol. Cell. Biol., 5(7):1750-1759 (1985) or Howley et al., U.S. Pat. No. 4,419,446. Another suitable mammalian cell line is the monkey COS-1 cell line. A similarly useful mammalian cell line is the CV-1 cell line.

Where desired, insect cells may be utilized as host cells in the method of the present invention. See, e.g., Miller et al, Genetic Engineering, 8:277-298 (Plenum Press 1986) and references cited therein. In addition, general methods for expression of foreign genes in insect cells using Baculovirus vectors are described in: Summers, M. D. and Smith, G. E. (1987) - A manual of methods for Baculovirus vectors and insect cell culture procedures, Texas Agricultural Experiment Station Bulletin No. 1555. An expression vector is constructed comprising a Baculovirus transfer vector, in which a

strong Baculovirus promoter (such as the polyhedron promoter) drives transcription of a eukaryotic secretion signal peptide coding region, which is translationally fused to the coding region for the fusion polypeptide.

5 For example, the plasmid pVL1392 (obtained from Invitrogen Corp., San Diego, California) can be used. After construction of the vector carrying the gene encoding the fusion polypeptide, two micrograms of this DNA is cotransfected with one microgram of Baculovirus

10 DNA (see Summers & Smith, 1987) into insect cells, strain SF9. Pure recombinant Baculovirus carrying the fusion molecule is used to infect cells cultured, for example, in Excell 401 serum-free medium (JRH Biosciences, Lenexa, Kansas). The fusion molecule secreted into the medium

15 can be recovered by standard biochemical approaches. Supernatants from mammalian or insect cells expressing the fusion protein can be first concentrated using any of an number of commercial concentration units.

The fusion molecules of the present invention may be

20 useful in the treatment of diseases characterized by a decreased levels of either myeloid, erythroid, lymphoid, or megakaryocyte cells of the hematopoietic system or combinations thereof. In addition, they may be used to activate mature myeloid and/or lymphoid cells. Among

25 conditions susceptible to treatment with the polypeptides of the present invention is leukopenia, a reduction in the number of circulating leukocytes (white cells) in the peripheral blood. Leukopenia may be induced by exposure to certain viruses or to radiation. It is often a side

30 effect of various forms of cancer therapy, e.g., exposure to chemotherapeutic drugs, radiation and of infection or hemorrhage. Therapeutic treatment of leukopenia with these fusion molecules of the present invention may avoid undesirable side effects caused by treatment with

35 presently available drugs.

The fusion molecules of the present invention may be useful in the treatment of neutropenia and, for example,

in the treatment of such conditions as aplastic anemia, cyclic neutropenia, idiopathic neutropenia, Chediak-Higashi syndrome, systemic lupus erythematosus (SLE), leukemia, myelodysplastic syndrome and myelofibrosis.

- 5 The fusion molecule of the present invention may be useful in the treatment or prevention of thrombocytopenia. Currently the only therapy for thrombocytopenia is platelet transfusions which are costly and carry the significant risks of infection (HIV, 10 HBV) and alloimmunization. The fusion molecule may alleviate or diminish the need for platelet transfusions. Severe thrombocytopenia may result from genetic defects such as Fanconi's Anemia, Wiscott-Aldrich, or May-Hegglin syndromes. Acquired thrombocytopenia may result from 15 auto- or allo-antibodies as in Immune Thrombocytopenia Purpura, Systemic Lupus Erythromatosis, hemolytic anemia, or fetal maternal incompatibility. In addition, splenomegaly, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, infection or 20 prosthetic heart valves may result in thrombocytopenia. Severe thrombocytopenia may also result from chemotherapy and/or radiation therapy or cancer. Thrombocytopenia may also result from marrow invasion by carcinoma, lymphoma, leukemia or fibrosis.
- 25 The fusion molecules of the present invention may be useful in the mobilization of hematopoietic progenitors and stem cells into peripheral blood. Peripheral blood derived progenitors have been shown to be effective in reconstituting patients in the setting of autologous 30 marrow transplantation. Hematopoietic growth factors including G-CSF and GM-CSF have been shown to enhance the number of circulating progenitors and stem cells in the peripheral blood. This has simplified the procedure for peripheral stem cell collection and dramatically 35 decreased the cost of the procedure by decreasing the number of pheresis required. The fusion molecule may be useful in mobilization of stem cells and further enhance

the efficacy of peripheral stem cell transplantation.

Another projected clinical use of growth factors has been in the in vitro activation of hematopoietic progenitors and stem cells for gene therapy. In order to have the gene of interest incorporated into the genome of the hematopoietic progenitor or stem cell one needs to stimulate cell division and DNA replication. Hematopoietic stem cells cycle at a very low frequency which means that growth factors may be useful to promote gene transduction and thereby enhance the clinical prospects for gene therapy.

Many drugs may cause bone marrow suppression or hematopoietic deficiencies. Examples of such drugs are AZT, DDI, alkylating agents and anti-metabolites used in chemotherapy, antibiotics such as chloramphenicol, penicillin, gancyclovir, daunomycin and sulfa drugs, phenothiazones, tranquilizers such as meprobamate, analgesics such as aminopyrine and dipyrone, anti convulsants such as phenytoin or carbamazepine, antithyroids such as propylthiouracil and methimazole and diuretics. The fusion molecules of the present invention may be useful in preventing or treating the bone marrow suppression or hematopoietic deficiencies which often occur in patients treated with these drugs.

Hematopoietic deficiencies may also occur as a result of viral, microbial or parasitic infections and as a result of treatment for renal disease or renal failure, e.g., dialysis. The fusion molecules of the present invention may be useful in treating such hematopoietic deficiency.

The treatment of hematopoietic deficiency may include administration of a pharmaceutical composition containing the fusion molecules to a patient. The fusion molecules of the present invention may also be useful for the activation and amplification of hematopoietic precursor cells by treating these cells in vitro with the fusion proteins of the present invention prior to

injecting the cells into a patient.

Various immunodeficiencies e.g., in T and/or B lymphocytes, or immune disorders, e.g., rheumatoid arthritis, may also be beneficially affected by treatment with the fusion molecules of the present invention. Immunodeficiencies may be the result of viral infections e.g. HTLV I, HTLV II, HTLV III, severe exposure to radiation, cancer therapy or the result of other medical treatment. The fusion molecules of the present invention may also be employed, alone or in combination with other hematopoietins, in the treatment of other blood cell deficiencies, including thrombocytopenia (platelet deficiency), or anemia. Other uses for these novel polypeptides are in the treatment of patients recovering from bone marrow transplants in vivo and ex vivo, and in the development of monoclonal and polyclonal antibodies generated by standard methods for diagnostic or therapeutic use.

Other aspects of the present invention are methods and therapeutic compositions for treating the conditions referred to above. Such compositions comprise a therapeutically effective amount of one or more of the fusion molecules of the present invention in a mixture with a pharmaceutically acceptable carrier. This composition can be administered either parenterally, intravenously or subcutaneously. When administered, the therapeutic composition for use in this invention is preferably in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such a parenterally acceptable protein solution, having due regard to pH, isotonicity, stability and the like, is within the skill of the art.

The dosage regimen involved in a method for treating the above-described conditions will be determined by the attending physician considering various factors which modify the action of drugs, e.g. the condition, body weight, sex and diet of the patient, the severity of any

infection, time of administration and other clinical factors. Generally, a daily regimen may be in the range of 0.2 - 150 µg/kg of fusion protein per kilogram of body weight. This dosage regimen is referenced to a standard level of biological activity which recognizes that native IL-3 generally possesses an EC₅₀ at or about 10 piconMolar to 100 piconMolar in the AML proliferation assay described herein. Therefore, dosages would be adjusted relative to the activity of a given fusion protein vs. the activity of native (reference) IL-3 and it would not be unreasonable to note that dosage regimens may include doses as low as 0.1 microgram and as high as 1 milligram per kilogram of body weight per day. In addition, there may exist specific circumstances where dosages of fusion molecule would be adjusted higher or lower than the range of 10 - 200 micrograms per kilogram of body weight. These include co-administration with other colony stimulating factor or IL-3 variant or growth factors; co-administration with chemotherapeutic drugs and/or radiation; the use of glycosylated fusion protein; and various patient-related issues mentioned earlier in this section. As indicated above, the therapeutic method and compositions may also include co-administration with other human factors. A non-exclusive list of other appropriate hematopoietins, CSFs, cytokines, lymphokines, hematopoietic growth factors and interleukins for simultaneous or serial co-administration with the polypeptides of the present invention includes GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, B-cell growth factor, B-cell differentiation factor and eosinophil differentiation factor, stem cell factor (SCF) also known as steel factor or c-kit ligand, or combinations thereof. The dosage recited above would be adjusted to compensate for such additional components in the therapeutic composition.

Progress of the treated patient can be monitored by periodic assessment of the hematological profile, e.g., differential cell count and the like.

The present invention is also directed to the following;

1. R_1-L-R_2 , R_2-L-R_1 , R_1-R_2 , R_2-R_1 , R_1-L-R_1 and R_1-R_1

wherein R1 is a human interleukin-3 mutant
10 polypeptide of the Formula:

	Ala	Pro	Met	Thr	Gln	Thr	Thr	Ser	Leu	Lys	Thr	Ser	Trp	Val	Asn
	1				5					10					15
15	Cys	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
					20					25					30
	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Asn	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
					35					40					45
20	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
					50					55					60
	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
25	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
					65					70					75
	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
					80					85					90
30	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
					95					100					105
	Xaa	Phe	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
					110					115					120
35	Xaa	Xaa	Xaa	Gln	Gln	Thr	Thr	Leu	Ser	Leu	Ala	Ile	Phe		
					125					130					

[SEQ ID NO:1]

wherein

- 5 Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or
 Arg;
- Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or
 Gln;
- Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or
 Cys;
- 10 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or
 Ala;
- Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,
 Gln, Asn, Thr, Ser or Val;
- Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp,
15 Asn, Gln, Leu, Val or Gly;
- Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys,
 Phe, Leu, Ser, or Arg;
- Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or
 Leu;
- 20 Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or
 Ala;
- Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or
 Trp;
- Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
- 25 Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
 Trp;
- Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;
- Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser,
 Leu, or Lys;
- 30 Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or
 Gln;
- Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala,
 or Glu;
- Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;
- 35 Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
 Thr, Arg, Ala, Phe, Ile or Met;
- Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or

Val;

- Xaa at position 36 is Asp, Leu, or Val;
- Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile;
- Xaa at position 38 is Asn, or Ala;
- 5 Xaa at position 40 is Leu, Trp, or Arg;
- Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro;
- Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, Val, Glu, Phe, Tyr, Ile, Met or Ala;
- 10 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg, Thr, Gly or Ser;
- Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala or Pro;
- Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His;
- 15 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;
- Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His;
- 20 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn;
- Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;
- Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, Ala, Ile, Val, His, Phe, Met or Gln;
- 25 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
- 30 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or Met;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala or Leu;
- Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- 35 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
- Xaa at position 57 is Asn or Gly;

- Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;
- Xaa at position 59 is Glu, Tyr, His, Leu, Pro, or Arg;
- Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr;
- 5 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
- Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;
- Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val;
- 10 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;
- Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;
- Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;
- 15 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His;
- Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;
- 20 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or Leu;
- Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, Trp, or Asn;
- 25 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;
- Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;
- Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- 30 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu;
- Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;
- Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;
- 35 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly,

- or Asp;
- Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu,
or Arg;
- 5 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val,
or Lys;
- Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu,
Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
- Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;
- Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
- 10 Xaa at position 85 is Leu, Asn, Val, or Gln;
- Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
- Xaa at position 87 is Leu, Ser, Trp, or Gly;
- Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
- Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,
15 Asn, or Ser;
- Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
or Met;
- Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
or His;
- 20 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala,
Gly, Ile or Leu;
- Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;
- Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln,
25 Lys, His, Ala, or Pro;
- Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly,
Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;
- Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;
- 30 Xaa at position 98 is His, Ile, A, Leu, Asp, Ala, Thr,
Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
Gly, Ser, Phe, or His;
- Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
35 Gln, or Pro;
- Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;

- Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- Xaa at position 103 is Asp, or Ser;
- Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
- 5 Leu, Gln, Lys, Ala, Phe, or Gly;
- Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, Leu, Lys, Ile, Asp, or His;
- Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;
- 10 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, Ser, Ala or Pro;
- Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly;
- Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln,
- 15 His, Glu, Ser, Ala, or Trp;
- Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;
- Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or Phe;
- Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr,
- 20 Asp, Lys, Leu, Ile, Val or Asn;
- Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu;
- Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, Trp, or Met;
- 25 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile;
- Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro;
- 30 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr;
- Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or Arg;
- Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or
- 35 Gln;
- Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or Gly;

Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;

Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr,
or Leu;

- 5 and which can additionally have Met- preceding the amino
acid in position 1; and wherein from 1 to 14 amino acids
can be deleted from the N-terminus and/or from 1 to 15
amino acids can be deleted from the C-terminus; and
wherein from 4 to 44 of the amino acids designated by Xaa
10 are different from the corresponding amino acids of
native (1-133) human interleukin-3;

2. The fusion protein of 1 wherein said human
interleukin-3 mutant polypeptide is of the Formula:

15 Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
1 5 10 15

Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Xaa Leu Lys Xaa Xaa
20 25 30

Xaa Xaa Xaa Xaa Xaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa Xaa
35 40 45

Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu Xaa
25 50 55 60

Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile Glu
65 70 75

30 Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr Ala
80 85 90

Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa Xaa
95 100 105

35 Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Xaa Leu Glu Xaa
110 115 120

Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe

125

130

[SEQ ID NO:2]

5

wherein

- Xaa at position 17 is Ser, Gly, Asp, Met, or Gln;
- Xaa at position 18 is Asn, His, or Ile;
- Xaa at position 19 is Met or Ile;
- 10 Xaa at position 21 is Asp or Glu;
- Xaa at position 23 is Ile, Ala, Leu, or Gly;
- Xaa at position 24 is Ile, Val, or Leu;
- Xaa at position 25 is Thr, His, Gln, or Ala;
- Xaa at position 26 is His or Ala;
- 15 Xaa at position 29 is Gln, Asn, or Val;
- Xaa at position 30 is Pro, Gly, or Gln;
- Xaa at position 31 is Pro, Asp, Gly, or Gln;
- Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu;
- 20 Xaa at position 33 is Pro or Glu;
- Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Ala, Arg, Gln, Glu, Ile, Phe, Thr or Met;
- Xaa at position 35 is Leu, Ala, Asn, Pro, Gln, or Val;
- Xaa at position 37 is Phe, Ser, Pro, or Trp;
- 25 Xaa at position 38 is Asn or Ala;
- Xaa at position 42 is Gly, Asp, Ser, Cys, Ala, Asn, Ile, Leu, Met, Tyr or Arg;
- Xaa at position 44 is Asp or Glu;
- Xaa at position 45 is Gln, Val, Met, Leu, Thr, Ala, Asn, Glu, Ser or Lys;
- 30 Xaa at position 46 is Asp, Phe, Ser, Thr, Ala, Asn Gln, Glu, His, Ile, Lys, Tyr, Val or Cys;
- Xaa at position 50 is Glu, Ala, Asn, Ser or Asp;
- Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- 35 Xaa at position 54 is Arg or Ala;
- Xaa at position 55 is Arg, Thr, Val, Leu, or Gly;

- Xaa at position 56 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
Glu, Leu, Thr, Val or Lys;
- Xaa at position 60 is Ala or Ser;
- Xaa at position 62 is Asn, Pro, Thr, or Ile;
- 5 Xaa at position 63 is Arg or Lys;
- Xaa at position 64 is Ala or Asn;
- Xaa at position 65 is Val or Thr;
- Xaa at position 66 is Lys or Arg;
- Xaa at position 67 is Ser, Phe, or His;
- 10 Xaa at position 68 is Leu, Ile, Phe, or His;
- Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, or
Gly;
- Xaa at position 71 is Ala, Pro, or Arg;
- Xaa at position 72 is Ser, Glu, Arg, or Asp;
- 15 Xaa at position 73 is Ala or Leu;
- Xaa at position 76 is Ser, Val, Ala, Asn, Glu, Pro, or
Gly;
- Xaa at position 77 is Ile or Leu;
- Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
20 Gly, or Asp;
- Xaa at position 80 is Asn, Gly, Glu, or Arg;
- Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
- Xaa at position 83 is Pro or Thr;
- 25 Xaa at position 85 is Leu or Val;
- Xaa at position 87 is Leu or Ser;
- Xaa at position 88 is Ala or Trp;
- Xaa at position 91 is Ala or Pro;
- Xaa at position 93 is Thr, Asp, Ser, Pro, Ala, Leu, or
30 Arg;
- Xaa at position 95 is His, Pro, Arg, Val, Leu, Gly, Asn,
Phe, Ser or Thr;
- Xaa at position 96 is Pro or Tyr;
- Xaa at position 97 is Ile or Val;
- 35 Xaa at position 98 is His, Ile, Asn, Leu, Ala, Thr, Leu,
Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;
- Xaa at position 99 is Ile, Leu, or Val;

40

- Xaa at position 100 is Lys, Arg, Ile, Gln, Pro, or Ser;
 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Pro,
 Asn, Ile, Leu or Tyr;
 Xaa at position 104 is Trp or Leu;
 5 Xaa at position 105 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr,
 Leu, Lys, Ile, Asp, or His;
 Xaa at position 106 is Glu or Gly;
 Xaa at position 108 is Arg, Ala, or Ser;
 Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;
 10 Xaa at position 112 is Thr, Val, or Gln;
 Xaa at position 114 is Tyr or Trp;
 Xaa at position 115 is Leu or Ala;
 Xaa at position 116 is Lys, Thr, Val, Trp, Ser, Ala, His,
 Met, Phe, Tyr or Ile;
 15 Xaa at position 117 is Thr or Ser;
 Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Asp, or
 Gly;
 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
 20 His, Ile, Tyr, or Cys;
 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr,
 or Leu;
- and which can additionally have Met- preceding the amino
 25 acid in position 1; and wherein from 1 to 14 amino acids
 can be deleted from the N-terminus and/or from 1 to 15
 amino acids can be deleted from the C-terminus; and
 wherein from 4 to 35 of the amino acids designated by Xaa
 are different from the corresponding amino acids of
 30 native (1-133) human interleukin-3.

3. The fusion protein of 2 wherein said human
 interleukin-3 mutant polypeptide is of the Formula:

35 Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
 1 5 10 15

41

Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa Xaa
 20 25 30
 Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa
 5 35 40 45
 Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala
 50 55 60
 10 Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu
 65 70 75
 Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala
 80 85 90
 15 Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Xaa Gly Asp Trp Xaa
 95 100 105
 Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu Xaa
 20 110 115 120
 Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
 125 130

[SEQ ID NO:3]

25

wherein

- Xaa at position 17 is Ser, Gly, Asp, or Gln;
- Xaa at position 18 is Asn, His, or Ile;
- Xaa at position 23 is Ile, Ala, Leu, or Gly;
- 30 Xaa at position 25 is Thr, His, or Gln;
- Xaa at position 26 is His or Ala;
- Xaa at position 29 is Gln or Asn;
- Xaa at position 30 is Pro or Gly;
- Xaa at position 32 is Leu, Arg, Asn, or Ala;
- 35 Xaa at position 34 is Leu, Val, Ser, Ala, Arg, Gln, Glu,
 Ile, Phe, Thr, or Met;
- Xaa at position 35 is Leu, Ala, Asn, or Pro;

- Xaa at position 38 is Asn or Ala;
Xaa at position 42 is Gly, Asp, Ser, Ala, Asn, Ile, Leu,
Met, Tyr or Arg;
Xaa at position 45 is Gln, Val, Met, Leu, Ala, Asn, Glu,
5 or Lys;
Xaa at position 46 is Asp, Phe, Ser, Gln, Glu, His, Val
or Thr;
Xaa at position 50 is Glu Asn, Ser or Asp;
Xaa at position 51 is Asn, Arg, Pro, Thr, or His;
10 Xaa at position 55 is Arg, Leu, or Gly;
Xaa at position 56 is Pro, Gly, Ser, Ala, Asn, Val, Leu
or
Gln;
Xaa at position 62 is Asn, Pro, or Thr;
15 Xaa at position 64 is Ala or Asn;
Xaa at position 65 is Val or Thr;
Xaa at position 67 is Ser or Phe;
Xaa at position 68 is Leu or Phe;
Xaa at position 69 is Gln, Ala, Glu, or Arg;
20 Xaa at position 76 is Ser, Val, Asn, Pro, or Gly;
Xaa at position 77 is Ile or Leu;
Xaa at position 79 is Lys, Gly, Asn, Met, Arg, Ile, or
Gly;
Xaa at position 80 is Asn, Gly, Glu, or Arg;
25 Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
His, Met, Phe, Ser, Thr, Tyr or Val;
Xaa at position 87 is Leu or Ser;
Xaa at position 88 is Ala or Trp;
Xaa at position 91 is Ala or Pro;
30 Xaa at position 93 is Thr, Asp, or Ala;
Xaa at position 95 is His, Pro, Arg, Val, Gly, Asn, Ser
or
Thr;
Xaa at position 98 is His, Ile, Asn, Ala, Thr, Gln, Glu,
35 Lys, Met, Ser, Tyr, Val or Leu;
Xaa at position 99 is Ile or Leu;
Xaa at position 100 is Lys or Arg;

- Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Pro, Asn, Ile, Leu or Tyr;
- Xaa at position 105 is Asn, Pro, Ser, Ile or Asp;
- Xaa at position 108 is Arg, Ala, or Ser;
- 5 Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;
- Xaa at position 112 is Thr or Gln;
- Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, Tyr or Ile;
- Xaa at position 117 is Thr or Ser;
- 10 Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
- Xaa at position 121 is Ala, Ser, Ile, Pro, or Asp;
- Xaa at position 122 is Gln, Met, Trp, Phe, Pro, His, Ile, or Tyr;
- Xaa at position 123 is Ala, Met, Glu, Ser, or Leu;
- 15

and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15 amino acids can be deleted from the C-terminus; and

20 wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133)human interleukin-3.

4. The fusion protein of 3 wherein said
- 25 human interleukin-3 mutant polypeptide is of the Formula:

- Xaa at position 42 is Gly, Asp, Ser, Ile, Leu, Met, Tyr, or Ala;
- 30 Xaa at position 45 is Gln, Val, Met or Asn;
- Xaa at position 46 is Asp, Ser, Gln, His or Val;
- Xaa at position 50 is Glu or Asp;
- Xaa at position 51 is Asn, Pro or Thr;
- Xaa at position 62 is Asn or Pro;
- 35 Xaa at position 76 is Ser, or Pro;
- Xaa at position 82 is Leu, Trp, Asp, Asn Glu, His, Phe, Ser or Tyr;

Xaa Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 95 100 105

5 Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:4]
 110

wherein

- Xaa at position 3 is Ser, Lys, Gly, Asp, Met, Gln, or Arg;
- 10 Xaa at position 4 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
- Xaa at position 5 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
- Xaa at position 6 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
- Xaa at position 7 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,
 Gln, Asn, Thr, Ser or Val;
- 15 Xaa at position 8 is Glu, Trp, Pro, Ser, Ala, His, Asp,
 Asn, Gln, Leu, Val, or Gly;
- Xaa at position 9 is Ile, Val, Ala, Leu, Gly, Trp, Lys,
 Phe, Leu, Ser, or Arg;
- Xaa at position 10 is Ile, Gly, Val, Arg, Ser, Phe, or
 20 Leu;
- Xaa at position 11 is Thr, His, Gly, Gln, Arg, Pro, or
 Ala;
- Xaa at position 12 is His, Thr, Phe, Gly, Arg, Ala, or
 Trp;
- 25 Xaa at position 13 is Leu, Gly, Arg, Thr, Ser, or Ala;
- Xaa at position 14 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
 Trp;
- Xaa at position 15 is Gln, Asn, Leu, Pro, Arg, or Val;
- Xaa at position 16 is Pro, His, Thr, Gly, Asp, Gln, Ser,
 30 Leu, or Lys;
- Xaa at position 17 is Pro, Asp, Gly, Ala, Arg, Leu, or
 Gln;
- Xaa at position 18 is Leu, Val, Arg, Gln, Asn, Gly, Ala,
 or Glu;
- 35 Xaa at position 19 is Pro, Leu, Gln, Ala, Thr, or Glu;
- Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
 Thr, Arg, Ala, Phe, Ile or Met;

- Xaa at position 21 is Leu, Ala, Gly, Asn, Pro, Gln, or Val;
- Xaa at position 22 is Asp, Leu, or Val;
- Xaa at position 23 is Phe, Ser, Pro, Trp, or Ile;
- 5 Xaa at position 24 is Asn, or Ala;
- Xaa at position 26 is Leu, Trp, or Arg;
- Xaa at position 27 is Asn, Cys, Arg, Leu, His, Met, Pro;
- Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Lys, Asn, Thr, Leu, Val, Glu, Phe, Tyr, Ile or Met;
- 10 Xaa at position 29 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg, Thr, Gly or Ser;
- Xaa at position 30 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala or Pro;
- Xaa at position 31 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, Asp, Asn, Arg, Ser, Ala, Ile, Glu, His or Trp;
- 15 Xaa at position 32 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;
- Xaa at position 33 is Ile, Gly, Val, Ser, Arg, Pro, or His;
- 20 Xaa at position 34 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn;
- Xaa at position 35 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;
- Xaa at position 36 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, Ala, Ile, Val, His, Phe, Met or Gln;
- 25 Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- Xaa at position 38 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
- 30 Xaa at position 39 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, Met, or;
- Xaa at position 40 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala or Leu;
- Xaa at position 41 is Arg, Thr, Val, Ser, Leu, or Gly;
- 35 Xaa at position 42 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
- Xaa at position 43 is Asn or Gly;

- Xaa at position 44 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;
- Xaa at position 45 is Glu, Tyr, His, Leu, Pro, or Arg;
- Xaa at position 46 is Ala, Ser, Pro, Tyr, Asn, or Thr;
- 5 Xaa at position 47 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
- Xaa at position 48 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;
- Xaa at position 49 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val;
- 10 Xaa at position 50 is Ala, Asn, Pro, Ser, or Lys;
- Xaa at position 51 is Val, Thr, Pro, His, Leu, Phe, or Ser;
- Xaa at position 52 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;
- 15 Xaa at position 53 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His;
- Xaa at position 54 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;
- 20 Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or Leu;
- Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala;
- Xaa at position 57 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, Trp, or Asn;
- 25 Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;
- Xaa at position 59 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;
- Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- 30 Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu;
- Xaa at position 62 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;
- Xaa at position 63 is Ile, Ser, Arg, Thr, or Leu;
- 35 Xaa at position 64 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,

- or Asp;
- Xaa at position 65 is Asn, Trp, Val, Gly, Thr, Leu, Glu,
or Arg;
- Xaa at position 67 is Leu, Gln, Gly, Ala, Trp, Arg, Val,
5 or Lys;
- Xaa at position 68 is Leu, Gln, Lys, Trp, Arg, Asp, Glu,
Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
- Xaa at position 69 is Pro, Ala, Thr, Trp, Arg, or Met;
- Xaa at position 70 is Cys, Glu, Gly, Arg, Met, or Val;
- 10 Xaa at position 71 is Leu, Asn, Val, or Gln;
- Xaa at position 72 is Pro, Cys, Arg, Ala, or Lys;
- Xaa at position 73 is Leu, Ser, Trp, or Gly;
- Xaa at position 74 is Ala, Lys, Arg, Val, or Trp;
- Xaa at position 75 is Thr, Asp, Cys, Leu, Val, Glu, His,
15 Asn, or Ser;
- Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
or Met;
- Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
or His;
- 20 Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala,
Gly, Ile or Leu;
- Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;
- Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln,
25 Lys, His, Ala or Pro;
- Xaa at position 81 is His, Gln, Pro, Arg, Val, Leu, Gly,
Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile or Tyr;
- Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- Xaa at position 83 is Ile, Val, Lys, Ala, or Asn;
- 30 Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr,
Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- Xaa at position 85 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
Gly, Ser, Phe, or His;
- Xaa at position 86 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
35 Gln, Pro;
- Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu or Gln;

- Xaa at position 88 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- Xaa at position 89 is Asp, or Ser;
- Xaa at position 90 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, Gln, Lys, Ala, Phe, or Gly;
- 5 Xaa at position 91 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, Leu, Lys, Ile, Asp, or His;
- Xaa at position 92 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;
- 10 Xaa at position 94 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, Ser, Ala, or Pro;
- Xaa at position 95 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly;
- Xaa at position 96 is Lys, Asn, Thr, Leu, Gln, Arg, His, Glu, Ser, Ala or Trp;
- 15 Xaa at position 97 is Leu, Ile, Arg, Asp, or Met;
- Xaa at position 98 is Thr, Val, Gln, Tyr, Glu, His, Ser, or Phe;
- Xaa at position 99 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, Lys, Leu, Ile, Val or Asn;
- 20 Xaa at position 100 is Tyr, Cys, His, Ser, Trp, Arg, or Leu;
- Xaa at position 101 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, Trp, or Met;
- 25 Xaa at position 102 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile;
- Xaa at position 103 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro;
- 30 Xaa at position 104 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr;
- Xaa at position 105 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or Arg;
- Xaa at position 106 is Asn, Ala, Pro, Leu, His, Val, or Gln;
- 35 Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or Gly;

50

Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;

Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr,
or Leu;

5

and which can additionally have Met- or Met-Ala-
preceding the amino acid in position 1; and wherein from
4 to 44 of the amino acids designated by Xaa are
different from the corresponding native amino acids of
10 (1-133) human interleukin-3;

R2 is a colony stimulating factor; and

L is a linker capable of Linking R1 to R2.

15

6. The fusion protein of 5 wherein said
human interleukin-3 mutant polypeptide is of the Formula:

20	1	5	10	15
	Asn Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Xaa Leu Lys Xaa			
	Xaa Xaa Xaa Xaa Xaa Xaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa			
	20	25	30	
25	Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu			
	35	40	45	
	Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile			
	50	55	60	
30	Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr			
	65	70	75	
35	Ala Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa			
	80	85	90	

51

Xaa Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Xaa Leu Glu

95

100

105

Xaa Xaa Xaa Xaa Gln Gln {SEQ ID NO:5}

5

110

wherein

- Xaa at position 3 is Ser, Gly, Asp, Met, or Gln;
- Xaa at position 4 is Asn, His, or Ile;
- 10 Xaa at position 5 is Met or Ile;
- Xaa at position 7 is Asp or Glu;
- Xaa at position 9 is Ile, Ala, Leu, or Gly;
- Xaa at position 10 is Ile, Val, or Leu;
- Xaa at position 11 is Thr, His, Gln, or Ala;
- 15 Xaa at position 12 is His or Ala;
- Xaa at position 15 is Gln, Asn, or Val;
- Xaa at position 16 is Pro, Gly, or Gln;
- Xaa at position 17 is Pro, Asp, Gly, or Gln;
- Xaa at position 18 is Leu, Arg, Gln, Asn, Gly, Ala, or
- 20 Glu;
- Xaa at position 19 is Pro or Glu;
- Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Ala, Arg,
- Gln, Glu, Ile, Phe, Thr or Met;
- Xaa at position 21 is Leu, Ala, Asn, Pro, Gln, or Val;
- 25 Xaa at position 23 is Phe, Ser, Pro, or Trp;
- Xaa at position 24 is Asn or Ala;
- Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Asn, Ile,
- Leu, Met Tyr or Arg;
- Xaa at position 30 is Asp or Glu;
- 30 Xaa at position 31 is Gln, Val, Met, Leu, Thr, Ala, Asn,
- Glu, Ser or Lys;
- Xaa at position 32 is Asp, Phe, Ser, Thr, Ala, Asn, Gln,
- Glu, His, Ile, Lys, Tyr, Val or Cys;
- Xaa at position 36 is Glu, Ala, Asn, Ser or Asp;
- 35 Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or
- His;
- Xaa at position 40 is Arg or Ala;

- Xaa at position 41 is Arg, Thr, Val, Leu, or Gly;
Xaa at position 42 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
Glu, Leu, Thr, Val Or Lys;
Xaa at position 46 is Ala or Ser;
- 5 Xaa at position 48 is Asn, Pro, Thr, or Ile;
Xaa at position 49 is Arg or Lys;
Xaa at position 50 is Ala or Asn;
Xaa at position 51 is Val or Thr;
Xaa at position 52 is Lys or Arg;
- 10 Xaa at position 53 is Ser, Phe, or His;
Xaa at position 54 is Leu, Ile, Phe, or His;
Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, or
Gly;
Xaa at position 57 is Ala, Pro, or Arg;
- 15 Xaa at position 58 is Ser, Glu, Arg, or Asp;
Xaa at position 59 is Ala or Leu;
Xaa at position 62 is Ser, Val, Ala, Asn, Glu, Pro, or
Gly;
Xaa at position 63 is Ile or Leu;
- 20 Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
Gly, or Asp;
Xaa at position 66 is Asn, Gly, Glu, or Arg;
Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
- 25 Xaa at position 69 is Pro or Thr;
Xaa at position 71 is Leu or Val;
Xaa at position 73 is Leu or Ser;
Xaa at position 74 is Ala or Trp;
Xaa at position 77 is Ala or Pro;
- 30 Xaa at position 79 is Thr, Asp, Ser, Pro, Ala, Leu, or
Arg;
Xaa at position 81 is His, Pro, Arg, Val, Leu, Gly, Asn,
Phe, Ser or Thr;
Xaa at position 82 is Pro or Tyr;
- 35 Xaa at position 83 is Ile or Val;
Xaa at position 84 is His, Ile, Asn, Leu, Ala, Thr, Leu,
Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;

53

- Xaa at position 85 is Ile, Leu, or Val;
 Xaa at position 86 is Lys, Arg, Ile, Gln, Pro, or Ser;
 Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Asn, Ile, Leu or Tyr;
- 5 Xaa at position 90 is Trp or Leu;
 Xaa at position 91 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr, Leu, Lys, Ile, Asp, or His;
 Xaa at position 92 is Glu, or Gly;
 Xaa at position 94 is Arg, Ala, or Ser;
- 10 Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
 Xaa at position 98 is Thr, Val, or Gln;
 Xaa at position 100 is Tyr or Trp;
 Xaa at position 101 is Leu or Ala;
 Xaa at position 102 is Lys, Thr, Val, Trp, Ser, Ala, His, Met, Phe, Tyr or Ile;
- 15 Xaa at position 103 is Thr or Ser;
 Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
 Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Asp, or Gly;
- 20 Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys;
 Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;
- 25 which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 35 of the amino acids designated by Xaa are different from the corresponding amino acids of native human interleukin-3.
- 30 7. The fusion protein of 6 wherein said human interleukin-3 mutant polypeptide is of the Formula:
- Asn Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa
 1 5 10 15
 Xaa Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp
 20 25 30

54

Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu
 35 40 45
 5 Ala Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile
 50 55 60
 Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr
 65 70 75
 10 Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Xaa Gly Asp Trp
 80 85 90
 Xaa Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu
 15 95 100 105

Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:6]
 110

wherein

- 20 Xaa at position 3 is Ser, Gly, Asp, or Gln;
 Xaa at position 4 is Asn, His, or Ile;
 Xaa at position 9 is Ile, Ala, Leu, or Gly;
 Xaa at position 11 is Thr, His, or Gln;
 Xaa at position 12 is His or Ala;
 25 Xaa at position 15 is Gln or Asn;
 Xaa at position 16 is Pro or Gly;
 Xaa at position 18 is Leu, Arg, Asn, or Ala;
 Xaa at position 20 is Leu, Val, Ser, Ala, Arg, Gln, Glu,
 Ile, Phe, Thr or Met;
 30 Xaa at position 21 is Leu, Ala, Asn, or Pro;
 Xaa at position 24 is Asn or Ala;
 Xaa at position 28 is Gly, Asp, Ser, Ala, Asn, Ile, Leu,
 Met, Tyr or Arg;
 Xaa at position 31 is Gln, Val, Met, Leu, Ala, Asn, Glu
 35 or
 Lys;
 Xaa at position 32 is Asp, Phe, Ser, Ala, Gln, Glu, His,

Val or Thr;

- Xaa at position 36 is Glu, Asn, Ser or Asp;
Xaa at position 37 is Asn, Arg, Pro, Thr, or His;
Xaa at position 41 is Arg, Leu, or Gly;
5 Xaa at position 42 is Pro, Gly, Ser, Ala, Asn, Val, Leu
or

Gln;

- Xaa at position 48 is Asn, Pro, or Thr;
Xaa at position 50 is Ala or Asn;
10 Xaa at position 51 is Val or Thr;
Xaa at position 53 is Ser or Phe;
Xaa at position 54 is Leu or Phe;
Xaa at position 55 is Gln, Ala, Glu, or Arg;
Xaa at position 62 is Ser, Val, Asn, Pro, or Gly;
15 Xaa at position 63 is Ile or Leu;
Xaa at position 65 is Lys, Asn, Met, Arg, Ile, or Gly;
Xaa at position 66 is Asn, Gly, Glu, or Arg;
Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
His, Met, Phe, Ser, Thr, Tyr or Val;
20 Xaa at position 73 is Leu or Ser;
Xaa at position 74 is Ala or Trp;
Xaa at position 77 is Ala or Pro;
Xaa at position 79 is Thr, Asp, or Ala;
Xaa at position 81 is His, Pro, Arg, Val, Gly, Asn, Ser
25 or

Thr;

- Xaa at position 84 is His, Ile, Asn, Ala, Thr, Arg, Gln,
Glu, Lys, Met, Ser, Tyr, Val or Leu;
Xaa at position 85 is Ile or Leu;
30 Xaa at position 86 is Lys or Arg;
Xaa at position 87 is Asp, Pro, Met, Lys, His, Pro, Asn,
Ile, Leu or Tyr;
Xaa at position 91 is Asn, Pro, Ser, Ile or Asp;
Xaa at position 94 is Arg, Ala, or Ser;
35 Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
Xaa at position 98 is Thr or Gln;
Xaa at position 102 is Lys, Val, Trp, or Ile;

Xaa at position 103 is Thr, Ala, His, Phe, Tyr or Ser;
Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
Xaa at position 107 is Ala, Ser, Ile, Pro, or Asp;
Xaa at position 108 is Gln, Met, Trp, Phe, Pro, His, Ile,
5 or Tyr;
Xaa at position 109 is Ala, Met, Glu, Ser, or Leu;

and which can additionally have Met- or Met-Ala-
preceding the amino acid in position 1; and wherein from
10 4 to 26 of the amino acids designated by Xaa are
different from the corresponding amino acids of native
(1-133)human interleukin-3.

8. The fusion protein of 7 wherein said
15 human interleukin-3 mutant polypeptide is of the Formula:

Xaa at position 17 is Ser, Lys, Asp, Met, Gln, or Arg;
Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or
Gln;
20 Xaa at position 19 is Met, Arg, Gly, Ala, or Cys;
Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or
Ala;
Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, or
Val;
25 Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, or
Gly;
Xaa at position 23 is Ile, Ala, Gly, Trp, Lys, Leu, Ser,
or Arg;
Xaa at position 24 is Ile, Gly, Arg, or Ser;
30 Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or
Ala;
Xaa at position 26 is His, Thr, Phe, Gly, Ala, or Trp;
Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
Xaa at position 28 is Lys, Leu, Gln, Gly, Pro, Val or
35 Trp;
Xaa at position 29 is Gln, Asn, Pro, Arg, or Val;
Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser,

- Leu, or Lys;
- Xaa at position 31 is Pro, Asp, Gly, Arg, Leu, or Gln;
- Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu;
- 5 Xaa at position 33 is Pro, Leu, Gln, Thr, or Glu;
- Xaa at position 34 is Leu, Gly, Ser, or Lys;
- Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, or Gln;
- Xaa at position 36 is Asp, Leu, or Val;
- Xaa at position 37 is Phe, Ser, or Pro;
- 10 Xaa at position 38 is Asn, or Ala;
- Xaa at position 40 is Leu, Trp, or Arg;
- Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, Pro;
- Xaa at position 42 is Gly, Asp, Ser, Cys, or Ala;
- Xaa at position 42 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
- 15 Cys, or Ser;
- Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, or Pro;
- Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, or Trp;
- 20 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, or Gly;
- Xaa at position 47 is Ile, Gly, Ser, Arg, Pro, or His;
- Xaa at position 48 is Leu, Ser, Cys, Arg, His, Phe, or Asn;
- Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
- 25 or Asp;
- Xaa at position 50 is Glu, Leu, Thr, Asp, or Tyr;
- Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
- 30 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, or Leu;
- 35 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, or Lys;
- Xaa at position 57 is Asn or Gly;

- Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;
- Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;
- Xaa at position 60 is Ala, Ser, Tyr, Asn, or Thr;
- 5 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
- Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, or Ile;
- Xaa at position 63 is Arg, Tyr, Trp, Ser, Pro, or Val;
- 10 Xaa at position 64 is Ala, Asn, Ser, or Lys;
- Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;
- Xaa at position 66 is Lys, Ile, Val, Asn, Glu, or Ser;
- Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His;
- 15 Xaa at position 68 is Leu, Val, Trp, Ser, Thr, or His;
- Xaa at position 69 is Gln, Ala, Pro, Thr, Arg, Trp, Gly, or Leu;
- Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 20 Xaa at position 71 is Ala, Met, Leu, Arg, Glu, Thr, Gln, Trp, or Asn;
- Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;
- Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;
- 25 Xaa at position 74 is Ile, Thr, Pro, Arg, Gly, Ala;
- Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, or Leu;
- Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;
- 30 Xaa at position 77 is Ile, Ser, Arg, or Thr;
- Xaa at position 78 is Leu, Ala, Ser, Glu, Gly, or Arg;
- Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Ile, or Asp;
- 35 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, or Arg;
- Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, or

Lys;

- Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, or Asp;
Xaa at position 83 is Pro, Thr, Trp, Arg, or Met;
Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
5 Xaa at position 85 is Leu, Asn, or Gln;
Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
Xaa at position 87 is Leu, Ser, Trp, or Gly;
Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,
10 or Asn;
Xaa at position 90 is Ala, Ser, Asp, Ile, or Met;
Xaa at position 91 is Ala, Ser, Thr, Phe, Leu, Asp, or
His;
Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, or
15 Leu;
Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;
Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, or
Pro;
20 Xaa at position 95 is His, Gln, Pro, Val, Leu, Thr or
Tyr;
Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
Xaa at position 97 is Ile, Lys, Ala, or Asn;
Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
25 or Pro;
Xaa at position 99 is Ile, Arg, Asp, Pro, Gln, Gly, Phe,
or His;
Xaa at position 100 is Lys, Tyr, Leu, His, Ile, Ser, Gln,
or Pro;
30 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, or Gln;
Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or
Pro;
Xaa at position 103 is Asp, or Ser;
35 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
Leu, Gln, Lys, Ala, Phe, or Gly;
Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,

60

Tyr, Leu, Lys, Ile, or His;

Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
or Pro;

Xaa at position 108 is Arg, Asp, Leu, Thr, Ile, or Pro;

5 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,
or Gly.

10 9. The fusion protein of 8 wherein said
human interleukin-3 mutant polypeptide is of the Formula:

```

      1           5           10
(Met)m-Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr
      15           20
Ser Trp Val Asn Cys Ser Xaa Xaa Xaa Asp Glu Ile Ile
15 25           30           35
Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa
      40           45           50
Xaa Asn Leu Asn Xaa Glu Asp Xaa Asp Ile Leu Xaa Glu
      55           60
20 Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa
      65           70           75
Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa
      80           85
Ile Leu Xaa Asn Leu Xaa Pro Cys Xaa Pro Xaa Xaa Thr
25 90           95           100
Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly
      105           110           115
Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu
      120           125
30 Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln Thr Thr Leu
      130
Ser Leu Ala Ile Phe [SEQ ID NO:7]

```

wherein m is 0 or 1; Xaa at position 18 is Asn or Ile;
35 Xaa at position 19 is Met, Ala or Ile; Xaa at position 20
is Ile, Pro or Ile; Xaa at position 23 is Ile, Ala or
Leu; Xaa at position 25 is Thr or His; Xaa at position 29
is Gln, Arg, Val or Ile; Xaa at position 32 is Leu, Ala,

61

Asn or Arg; Xaa at position 34 is Leu or Ser; Xaa at position 37 is Phe, Pro, or Ser; Xaa at position 38 is Asn or Ala; Xaa at position 42 is Gly, Ala, Ser, Asp or Asn; Xaa at position 45 is Gln, Val, or Met; Xaa at position 46 is Asp or Ser; Xaa at position 49 is Met, Ile, Leu or Asp; Xaa at position 50 is Glu or Asp; Xaa at position 51 is Asn Arg or Ser; Xaa at position 55 is Arg, Leu, or Thr; Xaa at position 56 is Pro or Ser; Xaa at position 59 is Glu or Leu; Xaa at position 60 is Ala or Ser; Xaa at position 62 is Asn, Val or Pro; Xaa at position 63 is Arg or His; Xaa at position 65 is Val or Ser; Xaa at position 67 is Ser, Asn, His or Gln; Xaa at position 69 is Gln or Glu; Xaa at position 73 is Ala or Gly; Xaa at position 76 is Ser, Ala or Pro; Xaa at position 79 is Lys, Arg or Ser; Xaa at position 82 is Leu, Glu, Val or Trp; Xaa at position 85 is Leu or Val; Xaa at position 87 is Leu, Ser, Tyr; Xaa at position 88 is Ala or Trp; Xaa at position 91 is Ala or Pro; Xaa at position 93 is Pro or Ser; Xaa at position 95 is His or Thr; Xaa at position 98 is His, Ile, or Thr; Xaa at position 100 is Lys or Arg; Xaa at position 101 is Asp, Ala or Met; Xaa at position 105 is Asn or Glu; Xaa at position 109 is Arg, Glu or Leu; Xaa at position 112 is Thr or Gln; Xaa at position 116 is Lys, Val, Trp or Ser; Xaa at position 117 is Thr or Ser; Xaa at position 120 is Asn, Gln, or His; Xaa at position 123 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native human interleukin-3.

30

10. The fusion protein of 9 wherein said human interleukin-3 mutant polypeptide is of the Formula:

	1	5	10
35	(Met _m -Ala _n) _p -Asn Cys Ser Xaa Xaa Xaa Asp Glu Xaa Ile		
	15	20	
	Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa		

wherein m is 0 or 1; n is 0 or 1; p is 0 or 1; Xaa at position 4 is Asn or Ile; Xaa at position 5 is Met, Ala or Ile; Xaa at position 6 is Ile, Pro or Leu; Xaa at position 9 is Ile, Ala or Leu; Xaa at position 11 is Thr or His; Xaa at position 15 is Gln, Arg, Val or Ile; Xaa at position 18 is Leu, Ala, Asn or Arg; Xaa at position 20 is Leu or Ser; Xaa at position 23 is Phe, Pro, or Ser; Xaa at position 24 is Asn or Ala; Xaa at position 28 is Gly, Ala, Ser, Asp or Asn; Xaa at position 31 is Gln, Val, or Met; Xaa at position 32 is Asp or Ser; Xaa at position 35 is Met, Ile or Asp; Xaa at position 36 is Glu or Asp; Xaa at position 37 is Asn, Arg or Ser; Xaa at position 41 is Arg, Leu, or Thr; Xaa at position 42 is Pro or Ser; Xaa at position 45 is Glu or Leu; Xaa at position 46 is Ala or Ser; Xaa at position 48 is Asn, Val or Pro; Xaa at position 49 is Arg or His; Xaa at position 51 is Val or Ser; Xaa at position 53 is Ser, Asn, His or Gln; Xaa at position 55 is Gln or Glu; Xaa at position 59 is Ala or Gly; Xaa at position 62 is Ser, Ala or Pro; Xaa at position 65 is Lys, Arg or Ser; Xaa at position 67 is Leu, Glu, or Val; Xaa at position 68 is Leu, Glu, Val or

Trp; Xaa at position 71 is Leu or Val; Xaa at position 73 is Leu, Ser or Tyr; Xaa at position 74 is Ala or Trp; Xaa at position 77 is Ala or Pro; Xaa at position 79 is Pro or Ser; Xaa at position 81 is His or Thr; Xaa at position 84 is His, Ile, or Thr; Xaa at position 86 is Lys or Arg; Xaa at position 87 is Asp, Ala or Met; Xaa at position 91 is Asn or Glu; Xaa at position 95 is Arg, Glu, Leu; Xaa at position 98 Thr or Gln; Xaa at position 102 is Lys, Val, Trp or Ser; Xaa at position 103 is Thr or Ser; Xaa at position 106 is Asn, Gln, or His; Xaa at position 109 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native (15-125)human interleukin-3.

11. The fusion protein of 10 wherein said human interleukin-3 mutant polypeptide is of the Formula:

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
Ala Glu Asp Val Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:9];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:10];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
5 Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:11];

10

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu
15 Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:12];

20

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
25 Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:13];

30

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Thr
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu
35 Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu

Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:14];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
5 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
10 Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:15];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
15 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
20 Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:16];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
25 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
30 His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:17];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
35 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln

Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln
5 [SEQ ID NO:18];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
10 Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
15 [SEQ ID NO:19];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
20 Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
25 [SEQ ID NO:20];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
30 Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln
35 [SEQ ID NO:21];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
5 Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:22];

10 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
15 Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:23];

20 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
25 Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:24];

30 Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His
Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu
Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg
Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu
Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
35 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln

Gln [SEQ ID NO:25];

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His
Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu
5 Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg
Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu
Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
10 Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:26];

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His
Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu
15 Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg
Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu
Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
20 Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
Gln [SEQ ID NO:27];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
25 Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu
Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro
Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
30 Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
Gln [SEQ ID NO:28];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
35 Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu

Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro
Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
Gln [SEQ ID NO:29];

5

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu
10 Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu
Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro
Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
Gln [SEQ ID NO:30];

15

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
20 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:31];

25

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
30 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:32];

35

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu

Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
5 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:33];

10 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
15 Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:34];

20 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
25 Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:35];

30 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
35 Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
Gln [SEQ ID NO:36];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
5 Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
10 Gln [SEQ ID NO:37];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
15 Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
20 Gln [SEQ ID NO:38];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg
25 Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
30 Gln [SEQ ID NO:39];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
35 Asn Ala Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg
Leu Ser Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro

Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:40]

5 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ala Ile His His
Leu Lys Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
10 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:41]

15 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
20 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:42]

25 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
30 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:43]

35

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu

Asn Asp Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
5 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:44]

10 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
15 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:45]

20 Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro
Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn
25 Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:46]

30

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
35 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro
Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys

Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln-Gln
[SEQ ID NO:47] and

5

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Leu Ile His His
Leu Lys Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu
Asn Ser Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
10 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:48].

15

The following are examples of the fusion proteins of
the presents invention:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
20 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
25 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val
30 Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
35 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr

Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:121]

5

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
10 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
15 Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
20 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
25 Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:122]

30

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
35 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln

Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
5 Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
10 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
15 [SEQ ID NO:123]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
20 Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
25 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
30 Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
35 Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu

Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:124]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
5 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
10 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu
15 Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met
Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
20 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln [SEQ ID NO:125]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
25 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
30 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu
35 Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met
Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala

Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln [SEQ ID NO:126]

5 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
10 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
15 Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu
Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met
Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
20 Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln [SEQ ID NO:127]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
25 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
30 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala
35 Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val

Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
5 Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
10 [SEQ ID NO:128]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
15 Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
20 Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala
Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
25 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
30 Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
35 [SEQ ID NO:129]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His

Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
5 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
10 Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala
Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
15 Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
20 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:130]

25
Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
30 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
35 Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu

Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
1 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
5 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
10 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
15 Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
20 Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
25 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:135]

25 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
30 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
35 Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu
Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met
Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe al Arg

Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
5 Gln Ala Gln Glu Gln Gln [SEQ ID NO:136]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
10 Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
15 Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu
Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu
20 Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val
Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
25 Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:137]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
30 Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
35 Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala

Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val
Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
5 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:131]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
10 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
15 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
20 Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu
Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val
Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
25 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:132]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
30 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
35 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser

Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu
Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
5 Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val
Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
10 Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:133]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
15 Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
20 Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
25 Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
30 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
35 [SEQ ID NO:134]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His

Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
5 Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
10 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:138]

15 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
20 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val
Asn Ala Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
25 Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly
Ser Glu Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Gly Asp
Phe Asp Tyr Glu Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
30 Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
35 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg

Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro

[SEQ ID NO:139]

5 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
10 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Pro Ala Arg Ser Pro Ser Pro
15 Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu Ala
Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met
Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln
Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln
Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr
20 Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro
Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe
Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp
Cys Trp Glu Pro Val Gln Glu [SEQ ID NO:141]

25 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
30 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val
Asn Ala Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
35 Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly
Ser Glu Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Gly Asp
Phe Asp Tyr Glu Asn Met Ala Pro Ala Arg Ser Pro Ser Pro

Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu Ala
Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met
Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln
Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln
5 Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr
Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro
Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe
Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp
Cys Trp Glu Pro Val Gln Glu [SEQ ID NO:142]

10 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
15 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Pro Val Asn Ala Gly Gly Gly Ser Gly Gly Gly
20 Ser Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly
Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Gly Gly Gly
Ser Gly Ser Gly Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Lys Leu Glu Gln Val
G Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
25 Lys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
30 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
35 [SEQ ID NO:143]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His

Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
5 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
10 Ser His Lys Ser Pro Asn Met Ala Pro Ala Arg Ser Pro Ser
Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu
Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu
Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu
Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys
15 Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu
Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr
Pro Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser
Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe
Asp Cys Trp Glu Pro Val Gln Glu [SEQ ID NO:144]
20
Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
25 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
30 Gly Gly Gly Ser Asn Met Ala Pro Val Pro Pro Gly Glu Asp
Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr Ser
Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly
Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met
Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn
35 Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly
Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu
Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe

Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr
 Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu
 Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu
 Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met
 5 Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln
 Ser Ser Leu Arg Ala Leu Arg Gln Met [SEQ ID NO:145]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
 10 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
 Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
 Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
 Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
 15 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
 Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
 Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
 20 Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
 Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala
 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro
 25 Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn
 Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
 Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
 Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
 Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 30 [SEQ ID NO:146]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
 35 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
 Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
 Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu

Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
5 Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
10 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
15 Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln

[SEQ ID NO:147]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
20 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
25 Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
30 Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Pro Gln Pro Pro
Val Asn Ala Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly
Gly Ser Glu Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Gly
35 Asp Phe Asp Tyr Glu Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu
Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu

Met Asp Arg Asn Leu Arg Leu Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
5 Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln. [SEQ ID NO:148]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
10 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
15 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
20 Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met
Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
25 Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
30 Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:149]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
35 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala

Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
5 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
10 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met
Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu
15 Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:150]
20
Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
25 Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
30 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gln Pro Pro Val Asn Ala Gly Gly Gly Ser Gly
35 Gly Gly Ser Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly
Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Gly
Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn Met Ala

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro
Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn
5 Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:151]

10 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
15 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser
20 Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
25 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
30 Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:152]

35

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu

Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
5 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu
10 Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met
Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg
Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
15 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln [SEQ ID NO:153]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
20 Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
25 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala
30 Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
35 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp

Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
5 [SEQ ID NO:154]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
10 Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
15 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu
Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu
20 Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val
Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
25 Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:155]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
30 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
35 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu

Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu Gly Gly Gly
Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met
5 Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
10 Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:156]

15 Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
20 Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
25 Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu Gly Gly Gly
Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met
30 Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
35 Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln

[SEQ ID NO:157]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
5 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
10 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
15 Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu Gly Gly Gly
Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
20 Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
25 [SEQ ID NO:158]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
30 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
35 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu

Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu Gly Gly Gly
Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
5 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
10 Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:159]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
15 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
20 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Ser Pro Ala Pro Pro Ala Cys
Asp Leu Arg Val Leu Ser Lys Leu Leu Arg Asp Ser His Val
25 Leu His Ser Arg Leu Ser Gln Cys Pro Glu Val His Pro Leu
Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe Ser Leu Gly
Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp Ile
Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala
Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly
30 Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr
Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His
Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly
Ser Thr Leu Cys Val Arg [SEQ ID NO:165]

35

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu

Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
5 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Ser Pro Ala Pro Pro Ala Cys
Asp Leu Arg Val Leu Ser Lys Leu Leu Arg Asp Ser His Val
10 Leu His Ser Arg Leu Ser Asn Cys Pro Glu Val His Pro Leu
Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe Ser Leu Gly
Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp Ile
Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala
Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly
15 Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr
Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His
Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly
Ser Thr Leu Cys Val Arg [SEQ ID NO:166]
20 Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu
Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu
Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu
Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln
25 Met Glu Glu Thr Lys Ala Gln Asp Ile Leu Gly Ala Val Thr
Leu Leu Leu Glu Gly Val Met Ala Ala Arg Gln Gln Leu Gly
Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln
Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro
30 Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys
Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val
Arg Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu
35 Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met
Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile

100

Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
 Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
 Gln Ala Gln Glu Gln Gln [SEQ ID NO:167]

5 Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu
 Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu
 Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu
 Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln
 10 Met Glu Glu Thr Lys Ala Gln Asp Ile Leu Gly Ala Val Thr
 Leu Leu Leu Glu Gly Val Met Ala Ala Arg Gln Gln Leu Gly
 Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln
 Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
 Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro
 15 Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys
 Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val
 Arg Glu Phe His Ala Tyr Val Glu Gly Gly Gly Gly Ser Pro
 Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala Asn Cys Ser
 Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro
 20 Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu
 Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly
 Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala
 25 Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu
 Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 [SEQ ID NO:168]

30 Materials and methods for fusion molecule Expression in E. coli

Unless noted otherwise, all specialty chemicals are obtained from Sigma Co., (St. Louis, MO). Restriction endonucleases, T4 poly-nucleotides kinase, E. coli DNA polymerase I large fragment (Klenow) and T4 DNA ligase are obtained from New England Biolabs (Beverly, Massachusetts).

35 Escherichia coli strains

Strain JM101: delta (pro lac), supE, thi, F' (traD38, rpoAB, lacI-Q, lacZdeltaM15) (Messing, 1979). This strain can be obtained from the American Type Culture Collection (ATCC), 12301 Parklawn Drive, Rockville, Maryland 20852, accession number 33876. MON105 (W3110 rpoH358) is a derivative of W3110 (Bachmann, 1972) and has been assigned ATCC accession number 55204. Strain GM48: dam-3, dcm-6, gal, ara, lac, thr, leu, tonA, tsx (Marinus, 1973) is used to make plasmid DNA that is not methylated at the sequence GATC.

Genes and plasmids

The gene used for hIL-3 production in *E. coli* is obtained from British Biotechnology Incorporated, Cambridge, England, catalogue number BBG14. This gene is carried on a pUC based plasmid designated pP0518. Many other human CSF genes can be obtained from R&D Systems, Inc. (Minn, MN) including IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, G-CSF, GM-CSF and LIF.

The plasmids used for production of hIL-3 in *E. coli* contain genetic elements whose use has been described (Olins et al., 1988; Olins and Rangwala, 1990). The replicon used is that of pBR327 (Covarrubias, et al., 1981) which is maintained at a copy number of about 100 in the cell (Soberon et al., 1980). A gene encoding the beta-lactamase protein is present on the plasmids. This protein confers ampicillin resistance on the cell. This resistance serves as a selectable phenotype for the presence of the plasmid in the cell.

For cytoplasmic expression vectors the transcription promoter is derived from the recA gene of *E. coli* (Sancar et al., 1980). This promoter, designated preCA, includes the RNA polymerase binding site and the lexA repressor binding site (the operator). This segment of DNA provides high level transcription that is regulated even when the recA promoter is on a plasmid with the pBR327 origin of replication (Olins et al., 1988) incorporated herein by reference.

The ribosome binding site used is that from gene 10 of phage T7 (Olins et al., 1988). This is encoded in a 100 base pair (bp) fragment placed adjacent to *precA*. In the plasmids used herein, the recognition sequence for the enzyme *NcoI* (CCATGG) follows the *g10-L*. It is at this *NcoI* site that the *hIL-3* genes are joined to the plasmid. It is expected that the nucleotide sequence at this junction will be recognized in mRNA as a functional start site for translation (Olins et al., 1988). The *hIL-3* genes used were engineered to have a *HindIII* recognition site (AAGCTT) downstream from the coding sequence of the gene. At this *HindIII* site is a 514 base pair *RsaI* fragment containing the origin of replication of the single stranded phage ϕ 1 (Dente et al., 1983; Olins, et al., 1990) both incorporated herein by reference. A plasmid containing these elements is pMON2341. Another plasmid containing these elements is pMON5847 which has been deposited at the American Type Culture Collection, 12301 Parklawn Drive, Rockville, Maryland 20852 under the accession number ATCC 68912.

In secretion expression plasmids the transcription promoter is derived from the *ara B*, *A*, and *D* genes of *E. coli* (Greenfield et al., 1978). This promoter is designated pAraBAD and is contained on a 323 base pair *SacII*, *BglIII* restriction fragment. The *LamB* secretion leader (Wong et al., 1988, Clement et al., 1981) is fused to the N-terminus of the *hIL-3* gene at the recognition sequence for the enzyme *NcoI* (5'CCATGG3'). The *hIL-3* genes used were engineered to have a *HindIII* recognition site (5'AAGCTT3') following the coding sequence of the gene.

Recombinant DNA methods

Synthetic gene assembly

The *hIL-3* variant genes and other CSF genes can be constructed by the assembly of synthetic oligonucleotides.

Synthetic oligonucleotides are designed so that they

would anneal in complementary pairs, with protruding single stranded ends, and when the pairs are properly assembled would result in a DNA sequence that encoded a portion of the desired gene. Amino acid substitutions in the hIL-3 gene are made by designing the oligonucleotides to encode the desired substitutions. The complementary oligonucleotides are annealed at concentration of 1 picomole per microliter in ligation buffer plus 50mM NaCl. The samples are heated in a 100 ml beaker of boiling water and permitted to cool slowly to room temperature. One picomole of each of the annealed pairs of oligonucleotides are ligated with approximately 0.2 picomoles of plasmid DNA, digested with the appropriate restriction enzymes, in ligation buffer (25 mM Tris pH 8.0, 10 mM MgCl₂, 10 mM dithiothreitol, 1 mM ATP, 2mM spermidine) with T4 DNA ligase obtained from New England Biolabs (Beverly, Massachusetts) in a total volume of 20 µl at room temperature overnight.

20 Polymerase Chain Reaction

Polymerase Chain Reaction (hereafter referred to as PCR) techniques (Saiki, 1985) used the reagent kit and thermal cycler from Perkin-Elmer Cetus (Norwalk, CT.). PCR is based on a thermostable DNA polymerase from 25 Thermus aquaticus. The PCR technique is a DNA amplification method that mimics the natural DNA replication process in that the number of DNA molecules doubles after each cycle, in a way similar to in vivo replication. The DNA polymerase mediated extension is in a 5' to 3' direction. The term "primer" as used herein refers to an oligonucleotide sequence that provides an end to which the DNA polymerase can add nucleotides that are complementary to a nucleotide sequence. The latter nucleotide sequence is referred to as the "template", to which the primers are annealed. The amplified PCR product is defined as the region comprised between the 5' ends of the extension primers. Since the primers have defined

sequences, the product will have discrete ends, corresponding to the primer sequences. The primer extension reaction is carried out using 20 picomoles (pmoles) of each of the oligonucleotides and 1 picogram of template plasmid DNA for 35 cycles (1 cycle is defined as 94 degrees C for one minute, 50 degrees C for two minutes and 72 degrees for three minutes.). The reaction mixture is extracted with an equal volume of phenol/chloroform (50% phenol and 50% chloroform, volume to volume) to remove proteins. The aqueous phase, containing the amplified DNA, and solvent phase are separated by centrifugation for 5 minutes in a microcentrifuge (Model 5414 Eppendorf Inc, Fremont CA.). To precipitate the amplified DNA the aqueous phase is removed and transferred to a fresh tube to which is added 1/10 volume of 3M NaOAc (pH 5.2) and 2.5 volumes of ethanol (100% stored at minus 20 degrees C). The solution is mixed and placed on dry ice for 20 minutes. The DNA is pelleted by centrifugation for 10 minutes in a microcentrifuge and the solution is removed from the pellet. The DNA pellet is washed with 70% ethanol, ethanol removed and dried in a speedvac concentrator (Savant, Farmingdale, New York). The pellet is resuspended in 25 microliters of TE (20mM Tris-HCl pH 7.9, 1mM EDTA). Alternatively the DNA is precipitated by adding equal volume of 4M NH₄OAc and one volume of isopropanol [Treco et al., (1988)]. The solution is mixed and incubated at room temperature for 10 minutes and centrifuged. These conditions selectively precipitate DNA fragments larger than ~ 20 bases and are used to remove oligonucleotide primers. One quarter of the reaction is digested with restriction enzymes [Higuchi, (1989)] and on completion heated to 70 degrees C to inactivate the enzymes.

Recovery of recombinant plasmids from ligation mixes

E. coli JM101 cells are made competent to take up

DNA. Typically, 20 to 100 ml of cells are grown in LB medium to a density of approximately 150 Klett units and then collected by centrifugation. The cells are resuspended in one half culture volume of 50 mM CaCl_2 and held at 4°C for one hour. The cells are again collected by centrifugation and resuspended in one tenth culture volume of 50 mM CaCl_2 . DNA is added to a 150 microliter volume of these cells, and the samples are held at 4°C for 30 minutes. The samples are shifted to 42°C for one minute, one milliliter of LB is added, and the samples are shaken at 37°C for one hour. Cells from these samples are spread on plates containing ampicillin to select for transformants. The plates are incubated overnight at 37°C. Single colonies are picked, grown in LB supplemented with ampicillin overnight at 37°C with shaking. From these cultures DNA is isolated for restriction analysis.

Culture medium

LB medium (Maniatis et al., 1982) is used for growth of cells for DNA isolation. M9 minimal medium supplemented with 1.0% casamino acids, acid hydrolyzed casein, Difco (Detroit, Michigan) is used for cultures in which recombinant fusion molecule is produced. The ingredients in the M9 medium are as follows: 3g/liter KH_2PO_4 , 6g/l Na_2HPO_4 , 0.5 g/l NaCl , 1 g/l NH_4Cl , 1.2 mM MgSO_4 , 0.025 mM CaCl_2 , 0.2% glucose (0.2% glycerol with the AraBAD promoter), 1% casamino acids, 0.1 ml/l trace minerals (per liter 108 g $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 4.0 g $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$, 7.0 $\text{CoCl}_2 \cdot 2\text{H}_2\text{O}$, 7.0 g $\text{Na}_2\text{MoO}_4 \cdot 2\text{H}_2\text{O}$, 8.0 g $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, 2.0 g H_3BO_3 , 5.0 g $\text{MnSO}_4 \cdot \text{H}_2\text{O}$, 100 ml concentrated HCl). Bacto agar is used for solid media and ampicillin is added to both liquid and solid LB media at 200 micrograms per milliliter.

Production of fusion molecules in E. coli with vectors employing the recA promoter

E. coli strains harboring the plasmids of interest are grown at 37°C in M9 plus casamino acids medium with

shaking in a Gyrotory water bath Model G76 from New Brunswick Scientific (Edison, New Jersey). Growth is monitored with a Klett Summerson meter (green 54 filter), Klett Mfg. Co. (New York, New York). At a Klett value of approximately 150, an aliquot of the culture (usually one milliliter) is removed for protein analysis. To the remaining culture, nalidixic acid (10mg/ml) in 0.1 N NaOH is added to a final concentration of 50 µg/ml. The cultures are shaken at 37°C for three to four hours after addition of nalidixic acid. A high degree of aeration is maintained throughout the bacterial growth in order to achieve maximal production of the desired gene product. The cells are examined under a light microscope for the presence of inclusion bodies. One milliliter aliquots of the culture are removed for analysis of protein content.

Fractionation of E. coli cells producing fusion proteins in the cytoplasm

The first step in purification of the fusion molecules is to sonicate the cells. Aliquots of the culture are resuspended from cell pellets in sonication buffer: 10 mM Tris, pH 8.0, 1 mM EDTA, 50 mM NaCl and 0.1 mM PMSF. These resuspended cells are subjected to several repeated sonication bursts using the microtip from a Sonicator cell disrupter, Model W-375 obtained from Heat Systems-Ultrasonics Inc. (Farmingdale, New York). The extent of sonication is monitored by examining the homogenates under a light microscope. When nearly all of the cells are broken, the homogenates are fractionated by centrifugation. The pellets, which contain most of the inclusion bodies, are highly enriched for fusion proteins.

Methods: Extraction, Refolding and Purification of
Fusion Molecules Expressed as Inclusion Bodies in E.
coli.

These fusion proteins can be purified by a variety of
5 standard methods. Some of these methods are described in
detail in Methods in Enzymology, Volume 182 'Guide to
Protein Purification' edited by Murray Deutscher,
Academic Press, San Diego, CA (1990).

Fusion proteins which are produced as insoluble
10 inclusion bodies in E. coli can be solubilized in high
concentrations of denaturant, such as Guanidine HCl or
Urea including dithiothreitol or beta mercaptoethanol as
a reducing agent. Folding of the protein to an active
conformation may be accomplished via sequential dialysis
15 to lower concentrations of denaturant without reducing
agent.

In some cases the folded proteins can be affinity
purified using affinity reagents such as mAbs or receptor
subunits attached to a suitable matrix. Alternatively,
20 (or in addition) purification can be accomplished using
any of a variety of chromatographic methods such as: ion
exchange, gel filtration or hydrophobic chromatography or
reversed phase HPLC.

25 rhIL-3 SANDWICH ELISA

The fusion protein concentrations can be determined
using a sandwich ELISA based on an appropriate affinity
purified antibody. Microtiter plates (Dynatech Immulon
II) are coated with 150 μ l goat-anti-rhIL-3 at a
30 concentration of approximately 1 μ g/ml in 100 mM NaHCO₃,
pH 8.2. Plates are incubated overnight at room
temperature in a chamber maintaining 100% humidity.
Wells are emptied and the remaining reactive sites on the
plate are blocked with 200 μ l of solution containing 10
35 mM PBS, 3% BSA and 0.05% Tween 20, pH 7.4 for 1 hour at
37° C and 100% humidity. Wells are emptied and washed 4X
with 150 mM NaCl containing 0.05% Tween 20 (wash buffer).

Each well then receives 150 μ l of dilution buffer (10 mM PBS containing 0.1% BSA, 3.01% Tween 20, pH 7.4), containing rhIL-3 standard, control, sample or dilution buffer alone. A standard curve is prepared with concentrations ranging from 0.125 ng/ml to 5 ng/ml using a stock solution of rhIL-3 (concentration determined by amino acid composition analysis). Plates are incubated 2.5 hours at 37° C and 100% humidity. Wells are emptied and each plate is washed 4X with wash buffer. Each well then received 150 μ l of an optimal dilution (as determined in a checkerboard assay format) of goat anti-rhIL-3 conjugated to horseradish peroxidase. Plates are incubated 1.5 hours at 37° C and 100% humidity. Wells are emptied and each plate is washed 4X with wash buffer. Each well then received 150 μ l of ABTS substrate solution (Kirkegaard and Perry). Plates are incubated at room temperature until the color of the standard wells containing 5 ng/ml rhIL-3 had developed enough to yield an absorbance between 0.5-1.0 when read at a test wavelength of 410 nm and a reference wavelength of 570 nm on a Dynatech microtiter plate reader. Concentrations of immunoreactive rhIL-3 in unknown samples are calculated from the standard curve using software supplied with the plate reader.

The following examples will illustrate the invention in greater detail although it will be understood that the invention is not limited to these specific examples.

EXAMPLE 1

30

Construction of expression plasmid for fusion molecules

Construction of a plasmid encoding a fusion protein composed of the IL-3 variant protein found in the plasmid, pMON13288 (United States Patent Application Serial number PCT/US93/11197), followed by a factor Xa proteolytic cleavage site, followed by murine IgG 2b hinge region, in which the cysteines have replaced with

serines, as the polypeptide linker sequence between the two proteins of the fusion and followed by G-CSF. The plasmid, pMON13288, is digested with EcoRI (which is internal in the IL-3 variant gene) and HindIII (which is after the stop codons for the IL-3 variant) and the 3900 base pair EcoRI, HindIII restriction fragment is purified. The genetic elements derived from pMON13288 are the beta-lactamase gene (AMP), pBR327 origin of replication, recA promoter, g10L ribosome binding site, the bases encoding amino acids 15-105 of (15-125) IL-3 variant gene, and phage f1 origin of replication. Pairs of complementary synthetic oligonucleotides are designed to replace the portion of the IL-3 variant gene after the EcoRI site (bases encoding amino acids 106-125), DNA sequence encoding the factor Xa cleavage site, DNA sequence encoding the polypeptide linker and AflIII restriction site to allow for cloning of the second gene in the fusion. When properly assembled the oligonucleotides result in a DNA sequence, encoding the above mentioned components in-frame, with EcoRI and HindIII restriction ends. Within this DNA sequence unique restriction sites are also created to allow for the subsequent replacement of specific regions with a sequence that has similar function (e.g. . . . alternative polypeptide linker region). A unique SnaBI restriction site is created at the end of the 13288 gene which allows for the cloning of other genes in the C-terminus position of the fusion. A unique XmaI site is created between sequence encoding the factor Xa cleavage site and the region encoding the polypeptide linker. A unique AflIII site is created after the linker region that allows for the cloning of the N-terminal protein of the fusion. The 3900 base pair fragment from pMON13288 is ligated with the assembled oligonucleotides and transformed into an appropriate E. coli strain. The resulting clones are screened by restriction analysis and DNA sequenced to confirm that the desired DNA sequence are created. The resulting plasmid is used as an

intermediate into which other genes can be cloned as a NcoI, HindIII fragment into the AflIII and HindIII sites to create the desired fusion. The overhangs created by NcoI and AflIII are compatible but the flanking sequence of the restriction recognition sites are different. The NcoI and AflIII sites are lost as a result of the cloning. The above mentioned restriction sites are used as examples and are not limited to those described. Other unique restriction site may also be engineered which serve the function of allowing the regions to be replaced. The plasmid encoding the resulting fusion is DNA sequenced to confirm that the desired DNA sequence is obtained. Other IL-3 variant genes or other colony stimulating factor genes can be altered in a similar manner by genetic engineering techniques to create the appropriate restriction sites which would allow for cloning either into the C-terminal or N-terminal position of the fusion construct described above. Likewise alternative peptidase cleavage sites or polypeptide linkers can be engineered into the fusion plasmids.

EXAMPLE 2

Expression, Extraction, Refolding and Purification of Fusion Proteins, such as pMON13061, Expressed as Inclusion Bodies in E. coli

E. coli strains harboring the plasmids of interest are grown overnight at 37°C and diluted the following morning, approximately 1/50, in fresh M9 plus casamino acids medium. The culture is grown at 37°C for three to four hours to mid-log (OD600=1) with vigorous shaking. Nalidixic acid (10mg/ml) in 0.1 N NaOH is added to a final concentration of 50 µg/ml. The cultures are grown at 37°C for three to four hours after the addition of nalidixic acid. A high degree of aeration is maintained throughout the bacterial growth in order to achieve maximal production of the desired fusion protein. In

cases where the fusion proteins are produced as insoluble inclusion bodies in E. coli the cells are examined under a light microscope for the presence of inclusion bodies.

E. coli cells containing fusion molecules in inclusion bodies were lysed by sonication. A 10% (w/v) suspension of the cells in 10 mM Tris-HCl pH 8.0 and 1 mM EDTA was subjected to three or four one minute bursts using a Sonicator cell disrupter, Model W-375, obtained from Heat Systems-Ultrasonics Inc. (Farmingdale, New York). The extent of cell disruption was monitored by examining the cells under a light microscope. When essentially all of the cells had been lysed, the inclusion bodies were harvested by centrifugation at 2800 x g for 20 min. The inclusion bodies were washed twice by suspending the inclusion body pellets to 10% in sonication buffer and centrifuging as above.

The fusion molecules were dissolved at one gram of inclusion bodies in 10 ml of 8 M urea with 50 mM Tris-HCl pH 9.5 and 5 mM DTT by blending with a Bio Homogenizer for 10 - 30 seconds and then gently stirring at 4°C for 1 - 2 hours. The dissolved fusion protein was clarified by centrifugation at 47,000 x g for 15 minutes.

Folding of the protein into an active conformation was done by diluting 8 fold with 2.3 M urea in 10 mM Tris-HCl pH 9.5 over 30 minutes to lower the concentration to 3 M urea. Folding of the fusion molecule was normally done between 2 and 3 M urea although higher concentrations of urea will also permit folding. The fusion was gently stirred under these conditions exposed to air until protein folding and formation of disulfide bonds was complete. The folding progress was monitored by reversed phase high performance liquid chromatography (RP - HPLC) using a 0.46 x 15 cm Vydac C 4 column (Hesperia, California) with a linear 35% to 65% acetonitrile (CH₃CN) / 0.1% trifluoroacetic acid (TFA) gradient over 25 minutes at 1 ml/minute.

After folding was complete, the pH of the fusion protein solution was lowered to 5.0 with glacial acetic acid and incubated at 4°C. After one hour, the solution was clarified by centrifugation at 47,000 x g for 15 minutes. The pH of the supernatant was lowered to 4.0 with acetic acid and clarified by filtration using a 0.45µ filter. The filtrate was dialyzed versus two, 100-fold, changes of 10 mM ammonium acetate pH 4.0. The pH of the dialyzed solution was increased to 6.5 with NaOH. The neutralized solution was then loaded at 2 mg of fusion protein per 1 ml of resin on a DEAE Fast Flow column (Pharmacia Piscataway, NJ) equilibrated with 10 mM Tris-Cl pH 6.5. The fusion protein was eluted using a linear gradient from 50 to 150 mM NaCl in equilibration buffer with a linear flow of 0.28 cm/min. for 12 hours. Using RP-HPLC analysis, fractions with a purity of 93% or better were pooled. The pooled fractions were dialyzed versus two, 100-fold, changes of 10 mM Tris-Cl pH 7.5. The dialyzed protein solution was sterile filtered, using a 0.45µ filter, and stored at 4°C. RP-HPLC and cation exchange chromatography such as CM Fast Flow can also be used separately or in combination with DEAE chromatography to purify the fusion proteins.

The purified fusion protein was analyzed by RP-HPLC, electrospray mass spectrometry, IEF, and SDS-PAGE. The protein quantitation was done by amino acid composition and Bradford protein determination.

In some cases the folded proteins can be affinity purified using affinity reagents such as mAbs or receptor subunits attached to a suitable matrix. Alternatively, (or in addition) purification can be accomplished using any of a variety of chromatographic methods such as: ion exchange, gel filtration or hydrophobic chromatography or reversed phase HPLC.

These and other protein purification methods are described in detail in Methods in Enzymology, Volume 182 'Guide to Protein Purification' edited by Murray

Deutscher, Academic Press, San Diego, CA (1990).

EXAMPLE 3

Determination of the in vitro activity of fusion proteins

5 The protein concentration of the fusion protein can
10 be determined using a sandwich ELISA based on an affinity
15 purified polyclonal antibody. Alternatively the protein
20 concentration can be determined by amino acid
25 composition. The bioactivity of the fusion molecule can
30 be determined in a number of in vitro assays compared
35 with native IL-3, the IL-3 variant or G-CSF alone or
 together. One such assay is the AML-193 cell
 proliferation assay. AML-193 cells respond to IL-3 and G-
 CSF which allows for the combined bioactivity of the IL-3
 variant/G-CSF fusion to be determined. In addition other
 factor dependent cell lines, such as M-NFS-60 (ATCC, CRL
 1838) or 32D which are murine IL-3 dependent cell line,
 may be used. The activity of IL-3 is species specific
 whereas G-CSF is not, therefore the bioactivity of the G-
 CSF component of the IL-3 variant/G-CSF fusion can be
 determined independently. The methylcellulose assay can
 be used to determine the effect of the IL-3 variant/G-CSF
 fusion protein on the expansion of the hematopoietic
 progenitor cells and the pattern of the different types
 of hematopoietic colonies in vitro. The methylcellulose
 assay can provide an estimate of precursor frequency
 since one measures the frequency of progenitors per
 100,000 input cells. Long term, stromal dependent
 cultures have been used to delineate primitive
 hematopoietic progenitors and stem cells. This assay can
 be used to determine whether the fusion molecule
 stimulates the expansion of very primitive progenitors
 and/or stem cells. In addition, limiting dilution
 cultures can be performed which will indicate the
 frequency of primitive progenitors stimulated by the
 fusion molecule.

The factor Xa cleavage site is useful to cleave the fusion protein after it is purified and re-folded to separate the IL-3 and G-CSF components of the fusion. After cleavage with factor Xa the IL-3 and G-CSF components of the fusion can be purified to homogeneity and assayed separately to demonstrate that both components are in an active conformation after being expressed, refolded and purified as a fusion.

EXAMPLE 4

Construction of pMON13018

Construction of pMON13018, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The 3900 base pair EcoRI, HindIII restriction fragment from pMON13288 was ligated with the following pairs of annealed complementary oligonucleotides:

Oligo #88Cterm1 [SEQ ID NO:91]

20 Oligo #88Cterm4 [SEO ID NO:92]

Oligo #88Xa2 [SEQ. ID NO:93]

Oligo #88Xa5 [SEQ ID NO:94]

25 Oligo #Glyn3 [SEQ ID NO:95]

Oligo #Glyn6 [SEQ ID NO:96]

The assembled oligonucleotides create EcoRI and HindIII restriction ends and the DNA sequence that encodes amino acids 106-125 of (15-125)hIL-3 variant 13288 and the polypeptide Linker 1 (Table 1) which is comprised of the factor Xa cleavage site and the amino acid sequence (Gly₃Ser)₂. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA was sequenced to determine that the sequence was that of

115

the oligonucleotides. A schematic diagram of the construction of the plasmid, pMON13018, is shown in Figure 2.

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EXAMPLE 5Construction of pMON13019

Construction of pMON13019, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The 4014 base pair XmaI/AflIII restriction fragment from pMON13018 was ligated with the following pair of annealed complementary oligonucleotides:

- 15 Oligo #IgG2b1 [SEQ ID NO:97]
Oligo #IgG2b2 [SEQ ID NO:98]

The assembled oligonucleotides create XmaI and AflIII restriction ends and the DNA sequence that encodes amino acids 9-33 of the polypeptide Linker 4 (Table 1) which is comprised of the factor Xa cleavage site and the murine IgG2b hinge region. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA was sequenced to determine that the sequence was that of the oligonucleotides.

EXAMPLE 6Construction of pMON13024

30 Construction of pMON13024, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The 4091 base pair NheI, HindIII restriction fragment from pMON13010 was ligated with the following pair of annealed complementary oligonucleotides:

Oligo #GCSFSna1 [SEQ ID NO:99]

116

Oligo #GCSFSna2 [SEQ ID NO:100]

The assembled oligonucleotides create NheI and HindIII restriction ends, create a SnaBI restriction site at the 3' end of the G-CSF gene, and the DNA sequence that encodes amino acids 155-175 of G-CSF. The stop codon after the G-CSF gene is eliminated and the DNA sequence of the SnaBI recognition site encodes amino acids Tyr Val in-frame at the C-terminus of G-CSF. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA was sequenced to determine that the sequence was that of the oligonucleotides.

15

EXAMPLE 7

Construction of pMON13027

Construction of pMON13027, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON13018, DNA was digested with restriction enzymes NcoI and SnaBI, resulting in a 3704 base pair NcoI, SnaBI fragment. Plasmid, pMON13024, DNA was digested with NcoI and SnaBI resulting in a 528 base pair NcoI, SnaBI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

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EXAMPLE 8

Construction of pMON13032

Construction of pMON13032, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON15930, DNA was digested with restriction enzymes NcoI and SnaBI,

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117

resulting in a 3829 base pair NcoI, SnaBI fragment. Plasmid, pMON13024, DNA was digested with NcoI and SnaBI, resulting in a 528 base pair NcoI, SnaBI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

EXAMPLE 9

Construction of pMON13041

Construction of pMON13041, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The 4018 base pair SnaBI/XmaI restriction fragment from pMON13018 was ligated with the following pair of annealed complementary oligonucleotides:

Oligo #Lysxa1 [SEQ ID NO:101]
Oligo #Lysxa2 [SEQ ID NO:102]

The assembled oligonucleotides create SnaBI and XmaI restriction ends and the DNA sequence that encodes amino acids 1-8 of the polypeptide Linker 2 (Table 1) which is comprised of the factor Xa cleavage site in which the Arg is changed to Lys and the amino acid sequence (Gly₃Ser)₂. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA was sequenced to determine that the sequence was that of the oligonucleotides.

EXAMPLE 10

Construction of pMON13042

Construction of pMON13042, an intermediate plasmid used

for constructing plasmids containing DNA sequences encoding fusion proteins. The 4018 base pair SnaBI/XmaI restriction fragment from pMON13018 was ligated with the following pair of annealed complementary
5 oligonucleotides:

Oligo #Glyxa1 [SEQ ID NO:103]

Oligo #Glyxa2 [SEQ ID NO:104]

10 The assembled oligonucleotides create SnaBI and XmaI restriction ends and the DNA sequence that encodes the polypeptide Linker 3 (Table 1). Polypeptide Linker 3 is comprised of the following amino acid sequence Tyr Val Glu Gly Gly Gly Gly Ser Pro (Gly₃Ser)₂ Asn [SEQ ID
15 NO:190]. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA was sequenced to determine that the sequence was that of the
20 oligonucleotides.

EXAMPLE 11

Construction of pMON13046

Construction of pMON13046, an intermediate plasmid used
25 for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON13018, DNA was digested with restriction enzymes NcoI and NsiI, resulting in a 3873 base pair NcoI,NsiI fragment. Plasmid, pMON13416 (United States Patent Application
30 Serial number PCT/US93/11197) DNA, which encodes a hIL-3 variant, was digested with NcoI and NsiI, resulting in a 170 base pair NcoI, NsiI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101.
35 Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the

119

correct insert.

EXAMPLE 12

Construction of pMON13047

- 5 Construction of pMON13047, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON13019, DNA was digested with restriction enzymes NcoI and NsiI, resulting in a 3918 base pair NcoI, NsiI fragment.
- 10 Plasmid, pMON13416, DNA was digested with NcoI and NsiI, resulting in a 170 base pair NcoI, NsiI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on
- 15 ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

EXAMPLE 13

Construction of pMON13478

- A pUC18 based plasmid containing the engineered gene encoding human granulocyte colony stimulating factor (hG-CSF) was obtained from R&D Systems (catalog # BBG13, Minneapolis MN). This plasmid was designated pMON13457.
- 25 The 3157 base pair ApaI, HindIII fragment from pMON13457 was ligated with the following pair of annealed complementary oligonucleotides:

- 30 Oligo #hgcsfma1 [SEQ ID NO:111]
Oligo #hgcsfma2 [SEQ ID NO:112]

- The assembled oligonucleotides create HindIII and ApaI restriction ends, an internal NcoI restriction site, the DNA sequence that encodes the first four amino acids of
- 35 hG-CSF (Thr Pro Leu Gly) preceded by an initiator methionine followed by an alanine. The methionine and alanine were added for expression in E. coli. The

ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert.

5 The resulting plasmid was designated pMON13478.

EXAMPLE 14

Construction of pMON13498

10 The 3163 base pair NcoI, ApaI fragment from pMON13478 was ligated with the following pair of annealed complementary oligonucleotides:

Oligo #hgcsfat3 [SEQ ID NO:115]

Oligo #hgcsfat4 [SEQ ID NO:116]

15

The assembled oligonucleotides create NcoI and ApaI restriction ends, and maximizes A/T content of the DNA sequence that encodes the first four amino acids of mature hG-CSF (Thr Pro Leu Gly). The A/T content of the DNA sequence was changed to increase protein expression levels in E. coli. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The ApaI restriction end of the oligonucleotides is compatible with the ApaI site but ApaI recognition sequence is altered. The resulting plasmid was designated pMON13498. The foregoing modifications to the hG-CSF gene are found in the DNA sequence [SEQ ID NO:178].

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EXAMPLE 15

Construction of pMON13010

Plasmid, pMON5743 (Olins and Rangwala [1990]), DNA was digested with restriction enzymes NcoI and EcoRI, resulting in a 3633 base pair NcoI, EcoRI fragment. Plasmid, pMON13498, DNA was digested with NcoI and EcoRI,

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resulting in a 542 base pair NcoI, EcoRI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, pMON13010, encodes the following amino acid sequence:

10 Peptide #

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe
15 Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp
20 Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly
Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
25 Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
30 Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala
Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val
Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro [SEQ ID NO:161]

35

DNA sequence # [SEQ ID NO:178] codes for the foregoing pMON13010 polypeptide.

EXAMPLE 16

40 Construction of pMON13499

The 3163 base pair NcoI, ApaI fragment from pMON13478 was ligated with the following pair of annealed complementary oligonucleotides:

45 Oligo #hgcsfat1 [SEQ ID NO:113]

Oligo #hgcsfat2 [SEQ ID NO:114]

The assembled oligonucleotides create NcoI and ApaI restriction ends, and maximizes A/T content of the DNA sequence that encodes the first three amino acids of hG-CSF (Thr Pro Leu). The A/T content of the DNA sequence was changed to increase expression levels in E. coli. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The resulting plasmid was designated pMON13499. The foregoing modifications to the hG-CSF gene are found in the DNA sequence [SEQ ID NO:177].

15 EXAMPLE 17

Construction of pMON13033

The 3117 base pair ApaI, BstXI fragment from pMON13499 was ligated with the following pair of annealed complementary oligonucleotides:

20 Oligo #gcys18 [SEQ ID NO:107]
Oligo #gcys181o [SEQ ID NO:108]

The assembled oligonucleotides create ApaI and BstXI restriction ends, and encodes amino acids 5 to 26 of hG-CSF except for amino acid 17 where the cysteine was replaced with serine. The cysteine was replaced with a serine to increase the in vitro refold efficiencies of the protein isolated from E. coli. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The resulting plasmid was designated pMON13033. The foregoing modifications to the hG-CSF gene are found in the DNA sequence [SEQ ID NO:179].

EXAMPLE 18Construction of pMON13037

Plasmid, pMON5743, DNA was digested with restriction
 5 enzymes NcoI and EcoRI, resulting in a 3633 base pair
 NcoI, EcoRI fragment. Plasmid, pMON13033, DNA was digested
 with NcoI and EcoRI, resulting in a 542 base pair NcoI,
 EcoRI fragment. The restriction fragments were ligated,
 and the ligation reaction mixture was used to transform
 10 E. coli K-12 strain JM101. Transformant bacteria were
 selected on ampicillin-containing plates. Plasmid DNA
 was isolated, analyzed by restriction analysis, and
 sequenced to confirm the correct insert. The plasmid,
 pMON13037, encodes the following amino acid sequence:

Peptide #

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe
 20 Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
 25 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp
 Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly
 Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
 30 Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
 Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
 Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
 35 Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala
 Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val
 40 Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 [SEQ ID NO:162]

DNA sequence # [SEQ ID NO:179] codes for the
 foregoing pMON13037 polypeptide.

EXAMPLE 19Construction of pMON13011

A pUC18 based plasmid containing the engineered gene encoding human granulocyte macrophage colony stimulating factor (hGM-CSF) was obtained from R&D Systems (catalog # BBG12, Minneapolis MN). This plasmid was designated pMON13458. The 2986 base pair NcoI, BsmI fragment from pMON13458 was ligated with the following pair of annealed complementary oligonucleotides:

Oligo #gm-aup [SEQ ID NO:105]

Oligo #gm-alow [SEQ ID NO:106]

The assembled oligonucleotides create NcoI and BsmI restriction ends and the DNA sequence that encodes the first nineteen amino acids of hGM-CSF. The DNA sequence encoding amino acids 3, 4, 5, 7, 9, 11, 12, 13 and 15 were changed to E.coli preferred codons to increase expression levels in E. coli. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The resulting plasmid was designated pMON13011. The foregoing modifications to the hGM-CSF gene are found in the DNA sequence [SEQ ID NO:176].

EXAMPLE 20Construction of pMON13012

Plasmid, pMON5743, DNA was digested with restriction enzymes NcoI and EcoRI, resulting in a 3633 base pair NcoI, EcoRI fragment. Plasmid, pMON13011, DNA was digested with NcoI and EcoRI, resulting in a 398 base pair NcoI, EcoRI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA

125

was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, pMON13012, encodes the following amino acid sequence:

5 Peptide

Met Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu
His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser
10 Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser
Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu
15 Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys
Gly Pro Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro
Pro Thr Pro Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu
20 Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe
Asp Cys Trp Glu Pro Val Gln Glu [SEQ ID NO:160]

25

DNA sequence # [SEQ ID NO:176] codes for the foregoing pMON13012 polypeptide.

30

EXAMPLE 21Construction of pMON5865

A pUC18 based plasmid containing the engineered gene encoding human interleukin-6 (hIL-6) was obtained from British Biotech (catalog # BBG17). The 3170 base pair
35 HindIII/BstXI fragment from this plasmid was ligated with the following pair of annealed complementary oligonucleotides:

Oligo #HIL6231 [SEQ ID NO:109]

40 Oligo #HIL6232 [SEQ ID NO:110]

The assembled oligonucleotides create HindIII and BstXI restriction ends and the DNA sequence that encodes the first ten amino acids of hIL-6 plus Met Ala at the N-
45 terminus for E. coli protein expression. The

126

oligonucleotides also create an NcoI site at the 5' end of the gene. The codons encoding the first ten amino acids were changed to *E. coli* preferred to increase expression levels in *E. coli*. The ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The resulting plasmid was designated pMON5865. The foregoing modifications to the hG-CSF gene are found in the DNA sequence [SEQ ID NO:175].

EXAMPLE 22

Construction of pMON13040

Plasmid pMON5743 DNA was digested with restriction enzymes NcoI and EcoRI, resulting in a 3633 base pair NcoI, EcoRI fragment. Plasmid, pMON5865, DNA was digested with NcoI and EcoRI, resulting in a 572 base pair NcoI, EcoRI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, pMON13040, encodes the following amino acid sequence:

Peptide #

Met Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala Ala
Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln
Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr
Cys Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala
Glu Asn Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys
Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile
Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn
Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser

127

Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu
 Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu
 5 Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr
 His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu
 Arg Ala Leu Arg Gln Met [SEQ ID NO:163]

10 DNA sequence # [SEQ ID NO:175] codes for the
 foregoing pMON13040 polypeptide.

EXAMPLE 23

15 Construction of pMON15931

Construction of pMON15931, an intermediate plasmid used
 for constructing plasmids containing DNA sequences
 encoding fusion proteins. The DNA sequence encoding the
 (Gly-Ser)-rich spacer region of the pIII protein of the
 20 filamentous bacteriophage fd (Schaller et al., 1975) was
 amplified using PCR techniques. A plasmid containing the
 gene encoding the pIII protein of the filamentous
 bacteriophage fd served as the template for the PCR
 reaction using the following oligonucleotides as primers:

25 Oligo # prefor [SEQ ID NO:117]

Oligo # revpre [SEQ ID NO:118]

The PCR primer extension reaction generated the following
 30 DNA sequence:

CCTGTCAACC CGGGCGGCGG CTCTGGTGGT GGTTCCTGGTG GCGGCTCTGA

GGGTGGCGGC TCTGAGGGTG GCGGTTCTGA GGGTGGCGGC TCTGAGGGTG

35 GCGGTTCCGG TGGCGGCTCC GGTTCGGTA ACATGTATTA TGA
 [SEQ ID NO:181]

40 The foregoing DNA sequence encodes amino acids 9 - 49 of
 the polypeptide Linker 7 (Table 1) which is comprised of
 the factor Xa cleavage site and the (Gly-Ser)-rich
 region of the pIII protein of the fd bacteriophage. The

128

PCR generated fragment was digested with XmaI and AflIII and ligated with the 4014 base pair XmaI, AflIII fragment from pMON13018. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant

- 5 bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

EXAMPLE 24

10 Construction of pMON15930

- Construction of pMON15930, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The DNA sequence encoding the (Gly-Ser)-rich spacer region with a few flanking amino
15 acids of the pIII protein of the filamentous bacteriophage fd (Schaller et al., 1975) was amplified using PCR techniques. A plasmid containing the gene encoding the pIII protein of the filamentous bacteriophage fd served as the template for the PCR
20 reaction using the following oligonucleotides as primers:

Oligo # forxtra [SEQ ID NO:119]

Oligo # xtrarev [SEQ ID NO:120]

- 25 The PCR primer extension reaction generated the following DNA sequence:

ATCGTCTGAC CTCCCGGGCC TCCTGTCAAT GCTGGCGGCG GCTCTGGTGG
30 TGGTTCTGGT GGCGGCTCTG AGGGTGGCGG CTCTGAGGGT GGCGGTTCTG
AGGGTGGCGG CTCTGAGGGT GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT
GATTTTGATT ATGAAAACAT GTCAAACGCT [SEQ ID NO:182]
35

- The foregoing DNA sequence encodes amino acids 9 - 70 of the polypeptide Linker 8 (Table 1) which is comprised of the factor Xa cleavage site and the (Gly-Ser)-rich region of the pIII protein of the fd bacteriophage. The
40 PCR generated fragment was digested with XmaI and AflIII

129

and ligated with the 4014 base pair XmaI, AflIII fragment from pMON13018. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

EXAMPLE 25

Construction of pMON13038

Construction of pMON13038, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON13019, DNA was digested with restriction enzymes NcoI and SnaBI, resulting in a 3749 base pair NcoI, SnaBI fragment. Plasmid, pMON13024, DNA was digested with NcoI and SnaBI, resulting in a 528 base pair NcoI, SnaBI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The resulting plasmid was designated pMON13038.

EXAMPLE 26

Construction of pMON13021

Plasmid, pMON13018, DNA was digested with restriction enzymes AflIII and HindIII, resulting in a 4023 base pair AflIII, HindIII fragment. Plasmid, pMON13288, DNA was digested with NcoI and HindIII, resulting in a 345 base pair NcoI, HindIII fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. A schematic diagram of the construction of the plasmid,

130

pMON13021, is shown in Figure 2. The plasmid, pMON13021, encodes the fusion with the following amino acid sequence:

5 Peptide # [SEQ ID NO:125]

DNA sequence # [SEQ ID NO:54] codes for the foregoing pMON13021 polypeptide.

10

EXAMPLE 27

Construction of pMON13022

Plasmid, pMON13018, DNA was digested with restriction enzymes AflIII and HindIII, resulting in a 4023 base pair AflIII, HindIII fragment. Plasmid, pMON13012, DNA was
15 digested with NcoI and HindIII, resulting in a 586 base pair NcoI, HindIII fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates.
20 Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, pMON13022, encodes the fusion with the following amino acid sequence:

25 Peptide # [SEQ ID NO:141]

DNA sequence # [SEQ ID NO:55] codes for the foregoing pMON13022 polypeptide.

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EXAMPLE 28-62

Further examples of fusion proteins, comprised in part of hIL-3 variant(s) are shown in Table 2. The plasmids
35 containing the genes encoding the fusion proteins in Table 2 were constructed by methods described in Materials and Methods and in Examples contained herein, particularly Examples 1, 9, 10, 26 and 27. DNA restriction fragments, indicated in Table 2 were ligated

and the resulting *E. coli* expression plasmids (Table 2) contain DNA sequences which encode the indicated polypeptide fusions (Table 2). The polypeptide fusions are comprised of two colony stimulating factors (R₁ and R₂) fused through a polypeptide linker (L) (Table 1), represented by the formula, R₁-L-R₂. Some of the genes encoding the polypeptide fusions in Table 2 were transferred from the *E. coli* expression vector, as a NcoI, HindIII restriction fragment into a mammalian cell (BHK) expression vector pMON3934. The *E. coli* and BHK expression plasmids are shown in Table 2. The biological activity, growth promoting activity in AML193.1:3 cells, for some of the polypeptide fusions in Table 2 is shown in Table 3. The biological activity, as evaluated in the methylcellulose assay, for some of the fusions in Table 2 is shown in Figures 3-7.

Table 1.
Polypeptide linker nomenclature and amino acid sequence.

Polypeptide Linker Designation	Amino Acid Sequence
Linker 1	YVIEGRISP(GGGS) ₂ N [SEQ ID NO:188]
Linker 2	YVIEGKISP(GGGS) ₂ N [SEQ ID NO:189]
Linker 3	YVEGGGGSP(GGGS) ₂ N [SEQ ID NO:190]
Linker 4	YVIEGRISPGEPSPGPISTINPSPPSKESHKSPN [SEQ ID NO:191]
Linker 5	YVIEGKISPGEPSPGPISTINPSPPSKESHKSPN [SEQ ID NO:192]
Linker 6	YVEGGGGSPGEPSPGPISTINPSPPSKESHKSPN [SEQ ID NO:193]

132

Linker 7	YVIEGRISP(GGGS)3(EGGGS)4GGGSGSGN [SEQ ID NO:194]
Linker 3	YVIEGRISPQPPVNA(GGGS)3(EGGGS)4GGGSGSGDFDYEN [SEQ ID NO:195]
Linker 9	EFHAYVEGGGGSP(GGGS)2N [SEQ ID NO:196]

Table 2

Example Number	Vector fragment	Insert fragment	E. coli PMON	BHK PMON	R1	Linker	R2	DNA [SEQ ID NO:]	Polypeptide [SEQ ID NO:]
28	PMON13018 4023 bp AclIII/HindIII	PMON13010 556 bp NcoI, HindIII	13021	3987	13288	Linker 1	G-CSF	[SEQ ID NO: 53]	[SEQ ID NO: 121]
26	PMON13018 4023 bp AclIII/HindIII	PMON13288 345 bp NcoI, HindIII	13021	3988	13288	Linker 1	13288	[SEQ ID NO: 54]	[SEQ ID NO: 125]
27	PMON13018 4023 bp AclIII/HindIII	PMON13012 412 bp NcoI, HindIII	13022	3989	13288	Linker 1	GN-CSF	[SEQ ID NO: 55]	[SEQ ID NO: 141]
29	PMON13021 4029 bp NcoI, SnaBI	PMON13024 528 bp NcoI, SnaBI	13026	3995	G-CSF	Linker 1	13288	[SEQ ID NO: 72]	[SEQ ID NO: 146]
10	PMON15911 4148 bp AclIII/HindIII	PMON13037 556 bp NcoI, HindIII	13062	26412	13288	Linker 8	G-CSF Ser17	[SEQ ID NO: 65]	[SEQ ID NO: 119]
11	PMON15911 4148 bp AclIII/HindIII	PMON13012 412 bp NcoI, HindIII	13011	3998	13288	Linker 8	GN-CSF	[SEQ ID NO: 66]	[SEQ ID NO: 142]
32	PMON15930 4119 bp AclIII/HindIII	PMON13010 556 bp NcoI, HindIII	15917	26405	13288	Linker 7	G-CSF	[SEQ ID NO: 67]	[SEQ ID NO: 143]
33	PMON13019 4068 bp AclIII/HindIII	PMON13010 556 bp NcoI, HindIII	13014	26406	13288	Linker 4	G-CSF	[SEQ ID NO: 68]	[SEQ ID NO: 129]
34	PMON13019 4068 bp AclIII/HindIII	PMON13012 412 bp NcoI, HindIII	13015	26407	13288	Linker 4	GN-CSF	[SEQ ID NO: 69]	[SEQ ID NO: 144]
35	PMON13019 4068 bp AclIII/HindIII	PMON13288 345 bp NcoI, HindIII	13036	26408	13288	Linker 4	13288	[SEQ ID NO: 62]	[SEQ ID NO: 111]
36	PMON13038 4257 bp AclIII/HindIII	PMON13288 345 bp NcoI, HindIII	13063	26433	G-CSF	Linker 4	13288	[SEQ ID NO: 73]	[SEQ ID NO: 150]
17	PMON13012 4337 bp AclIII/HindIII	PMON13288 345 bp NcoI, HindIII	13064	26434	G-CSF	Linker 8	13288	[SEQ ID NO: 74]	[SEQ ID NO: 151]
18	PMON13018 4023 bp AclIII/HindIII	PMON13037 556 bp NcoI, HindIII	13039	26415	13288	Linker 1	G-CSF Ser17	[SEQ ID NO: 56]	[SEQ ID NO: 122]
19	PMON13027 4212 bp AclIII/HindIII	PMON13416 345 bp NcoI, HindIII	13043	26416	G-CSF	Linker 1	13416	[SEQ ID NO: 75]	[SEQ ID NO: 147]

Table 2 cont

Example Number	vector fragment	Insert fragment	E. coli PMON	BIK PMON	R1	Linker	R2	DNA [SEQ ID NO:]	Polypeptide [SEQ ID NO:]
40	PMON13032 4337 bp AflIII/HindIII	PMON13416 345 bp NcoI, HindIII	13044	26417	G-CSF	Linker 8	13416	[SEQ ID NO: 76]	[SEQ ID NO: 148]
41	PMON13038 4257 bp AflIII/HindIII	PMON13416 345 bp NcoI, HindIII	13045	26418	G-CSF	Linker 4	13416	[SEQ ID NO: 77]	[SEQ ID NO: 149]
42	PMON13041 4023 bp AflIII, HindIII	PMON13037 556 bp NcoI, HindIII	13054	26424	13288	Linker 2	G-CSF Ser17	[SEQ ID NO: 59]	[SEQ ID NO: 123]
43	PMON13042 4023 bp AflIII, HindIII	PMON13037 556 bp NcoI, HindIII	13056	26426	13288	Linker 3	G-CSF Ser17	[SEQ ID NO: 60]	[SEQ ID NO: 124]
44	PMON13041 4023 bp AflIII, HindIII	PMON13288 345 bp NcoI, HindIII	13055	26425	13288	Linker 2	13288	[SEQ ID NO: 58]	[SEQ ID NO: 126]
45	PMON13042 4023 bp AflIII, HindIII	PMON13288 345 bp NcoI, HindIII	13057	26427	13288	Linker 3	13288	[SEQ ID NO: 61]	[SEQ ID NO: 127]
46	PMON13047 4068 bp AflIII, HindIII	PMON13416 345 bp NcoI, HindIII	13052	26422	13416	Linker 4	13416	[SEQ ID NO: 82]	[SEQ ID NO: 137]
47	PMON13047 4068 bp AflIII, HindIII	PMON13037 556 bp NcoI, HindIII	13053	26423	13416	Linker 4	G-CSF Ser17	[SEQ ID NO: 83]	[SEQ ID NO: 138]
48	PMON13023 4409 bp NsiI, NcoI	PMON13416 170 bp NcoI, NsiI	13066	26436	13416	Linker 1	G-CSF	[SEQ ID NO: 84]	[SEQ ID NO: 134]
49	PMON13046 4023 bp AflIII, HindIII	PMON13037 556 bp NcoI, HindIII	13051	26421	13416	Linker 1	G-CSF Ser17	[SEQ ID NO: 85]	[SEQ ID NO: 135]
50	PMON13046 4023 bp AflIII, HindIII	PMON13416 345 bp NcoI, HindIII	13050	26420	13416	Linker 1	13416	[SEQ ID NO: 86]	[SEQ ID NO: 136]
51	PMON13041 3994 bp XmaI, HindIII	PMON13034 630 bp XmaI, HindIII	13058	26428	13288	Linker 5	G-CSF	[SEQ ID NO: 70]	[SEQ ID NO: 129]
52	PMON13042 3994 bp XmaI, HindIII	PMON13034 630 bp XmaI, HindIII	13060	26430	13288	Linker 6	G-CSF	[SEQ ID NO: 71]	[SEQ ID NO: 130]
53	PMON13041 3994 bp XmaI, HindIII	PMON13036 419 bp XmaI, HindIII	13059	26429	13288	Linker 5	13288	[SEQ ID NO: 63]	[SEQ ID NO: 132]

Table 2 cont.

Example Number	vector fragment	Insert fragment	E. coli PMON	BHK PMON	R1	Linker	R2	DNA [SEQ ID NO:]	Polypeptide [SEQ ID NO:]
54	PMON13042 3994 bp XmaI, HindIII	PMON13036 419 bp XmaI, HindIII	11061	26431	13288	Linker 6	13288	[SEQ ID NO: 64]	[SEQ ID NO: 133]
55	PMON13018 4023 bp AflIII, HindIII	PMON13040 586 bp NcoI, HindIII	13049	26435	13288	Linker 1	IL 6	[SEQ ID NO: 57]	[SEQ ID NO: 145]
56	PMON13056 4409 bp NcoI, NsiI	PMON13416 170 bp NcoI, NsiI	13145		13416	Linker 3	G-CSF Ser17	[SEQ ID NO: 87]	[SEQ ID NO: 152]
57	PMON13053 4599 bp SnaBI, XmaI	GlyXa1 [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13146		13416	Linker 6	G-CSF Ser17	[SEQ ID NO: 89]	[SEQ ID NO: 154]
58	PMON13050 4343 bp SnaBI, XmaI	GlyXa1 [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13147		13416	Linker 3	13416	[SEQ ID NO: 88]	[SEQ ID NO: 151]
59	PMON13052 4388 bp SnaBI, XmaI	GlyXa1 [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13148		13416	Linker 6	13416	[SEQ ID NO: 90]	[SEQ ID NO: 155]
60	PMON13043 4532 bp SnaBI, XmaI	GlyXa1 [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13151		G-CSF	Linker 3	13416	[SEQ ID NO: 78]	[SEQ ID NO: 158]
61	PMON13151 4479 bp NcoI, BstXI	PMON13017 78 bp NcoI, BstXI	13149		G-CSF Ser17	Linker 3	13416	[SEQ ID NO: 80]	[SEQ ID NO: 159]
62	PMON13045 4577 bp SnaBI, XmaI	GlyXa1 [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13152		G-CSF	Linker 6	13416	[SEQ ID NO: 79]	[SEQ ID NO: 156]
63	PMON13152 4524 bp NcoI/BstXI	PMON13037 78 bp NcoI, BstXI	13150		G-CSF Ser17	Linker 6	13416	[SEQ ID NO: 81]	[SEQ ID NO: 157]

Example 635 Isolation of 1-332 and 1-153 amino acid forms of c-mpl ligand (Meg-CSF)

A. Reverse transcriptase reaction (c-mpl ligand sequence based on Genbank accession #L33410). Human fetal liver,
10 A+ RNA was obtained from Clontech (Palo Alto, CA). The first strand cDNA reactions was carried out using a cDNA Cycle™ Kit obtained from Invitrogen (San Diego, CA).

B. Polymerase chain reactions

15 Following the reverse transcriptase (RT) reaction, the 1-332 c-mpl ligand was amplified by PCR using the oligonucleotide primers c-mplNcoI [SEQ ID NO:169], which created an NcoI site immediately preceding the 5' end of the gene and c-mplEcoRI [SEQ ID NO:170] which created an
20 EcoRI site immediately 3' to the stop codon. Following the RT reaction, the 1-153 c-mpl ligand was amplified using the c-mplNcoI [SEQ ID NO:169] primer and the 3' primer, c-mplHindIII [SEQ ID NO:171] which created a stop codon and an HindIII site immediately 3' to the codon for
25 amino acid 153.

Example 64Construction of pMON26448

30 The 1-153 c-mpl ligand PCR product was digested with NcoI and HindIII restriction enzymes for subcloning into pMON3934. pMON3934, a mammalian expression vector, is derived from pMON3359 [Hippenmeyer et al., (1993)], but it contains a modified human IL 3 signal peptide sequence
35 in addition to the IE110 promoter and poly-A signal. The signal peptide sequence is flanked by BamHI and NcoI restriction enzyme sites, which facilitates cloning and

137

expression of genes as NcoI, HindIII fragments. The HindIII site is 3' to the NcoI site. The DNA sequence of the signal peptide is shown below (restriction enzyme sites are indicated above). The ATG (methionine) codon within the NcoI site is in-frame with the initiator ATG of the signal peptide (underlined);

BamHI
 10 GGATCCACCATGAGCCGCTGCCCGTCTCTGCTCCAACCTCTGGTCCGCCCC
 NcoI MetSerArgLeuProValLeuLeuLeuLeuGlnLeuLeuValArgPro
 GCCATGG [SEQ ID NO:140]
 AlaMet [SEQ ID NO:187]

15

The resulting plasmid was designated pMON26448. The plasmid, pMON26448, encodes the fusion with the following amino acid sequence:

20 Peptide #
 Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser
 Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln
 25 Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala
 Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr
 Lys Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly
 30 Val Met Ala Ala Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser
 Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala
 35 Leu Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr
 Thr Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His
 Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly Ser
 40 Thr Leu Cys Val Arg [SEQ ID NO:164]

DNA sequence # [SEQ ID NO:180] codes for the foregoing pMON26448 polypeptide.

45

EXAMPLE 65

Isolation of cDNA sequence amino acid 1-153 form of c-mpl ligand (Meg-CSF) with modified C-terminus

A. Reverse transcriptase reaction (c-mpl ligand sequence based on Genbank accession #L33410). Human fetal liver A+ RNA was obtained from Clontech (Palo Alto, CA). The first strand cDNA reactions was carried out using a cDNA Cycle™ Kit obtained from Invitrogen (San Diego, CA).

B. Polymerase chain reactions

Following the reverse transcriptase (RT) reaction, the 1-332 c-mpl ligand was amplified by PCR using the oligonucleotide primers c-mplNcoI [SEQ ID NO:169], which created an NcoI site immediately preceeding the 5' end of the gene and c-mplEcoRI [SEQ ID NO:170] which created an EcoRI site immediately 3' to the stop codon. Using the above PCR reaction as the template, the 1-153 c-mpl ligand was amplified using the c-mplNcoI [SEQ ID NO:169] primer and the 3' primer, Eco-mpl [SEQ ID NO:172] which created an EcoRI site immediately 3' to the codon for amino acid 153 and encodes the amino acids Glu Phe in-frame at the C-terminus of the gene. The 1-153 c-mpl ligand PCR product was digested with NcoI and EcoRI. The resulting 467 base pair NcoI, EcoRI restriction fragment was subsequently cloned into intermediate plasmids, described in the examples herein, to create fusion polypeptides.

Example 65Construction of pMON26460

5 Plasmid, pMON13018, DNA was digested with restriction
enzymes AflIII and HindIII, resulting in a 4023 base pair
AflIII, HindIII fragment. Plasmid, pMON26448, DNA was
digested with NcoI and HindIII, resulting in a 468 base
pair NcoI, HindIII fragment. The restriction fragments
10 were ligated, and the ligation reaction mixture was used
to transform E. coli. Transformant bacteria were
selected on ampicillin-containing plates. Plasmid DNA
was isolated, analyzed by restriction analysis, and
sequenced to confirm the correct insert. The E. coli
15 expression plasmid, pMON26460, encodes the fusion with
the following amino acid sequence:

Peptide # [SEQ ID NO:165]

20 DNA sequence # [SEQ ID NO:183] codes for the
foregoing pMON26460 polypeptide.
The gene encoding the fusion was transferred as a
NcoI, HindIII fragment to the mammalian expression vector,
pMON3934, and the resulting plasmid was designated
25 pMON26463.

Example 67Construction of pMON26461

30 The 4029 base pair NcoI, SnaBI fragment from, pMON13057,
was ligated with the 467 base pair NcoI, EcoRI PCR
generated fragment from Example 65 and two
oligonucleotides (Ecosna1 [SEQ ID NO:173], Ecosna2
[SEQ ID NO:174]) The ligation reaction mixture was used
35 to transform E. coli. Transformant bacteria were
selected on ampicillin-containing plates. Plasmid DNA
was isolated, analyzed by restriction analysis, and

140

sequenced to confirm the correct insert. The E. coli expression plasmid, pMON26461, encodes the fusion with the following amino acid sequence:

5 Peptide # [SEQ ID NO:168]

DNA sequence # [SEQ ID NO:186] codes for the foregoing pMON26461 polypeptide.

The gene encoding the fusion was transferred as a
10 NcoI,HindIII fragment to the mammalian expression vector, pMON3934, and the resulting plasmid was designated pMON26464.

Example 68

15 Construction of pMON26471

The 3285 base pair NcoI,HindIII fragment from, pMON3935, was ligated with the 362 base pair NcoI,SmaI restriction fragment from pMON26426 and the 494 base pair
20 SmaI,HindIII restriction fragment from pMON26460, and the ligation reaction mixture was used to transform E. coli. Transformant bacteria were selected on spectinomycin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The E. coli expression plasmid,
25 pMON26471, encodes the fusion with the following amino acid sequence:

Peptide # [SEQ ID NO:166]

30 DNA sequence # [SEQ ID NO:184] codes for the foregoing pMON26471 polypeptide.
The gene encoding the fusion was transferred as a NcoI,HindIII fragment to the mammalian expression vector, pMON3934, and the resulting plasmid was designated
35 pMON26473.

Example 69

Construction of pMON26472

The 3285 base pair NcoI,HindIII fragment from, pMON3935,

was ligated with the 481 base pair NcoI, SnaBI restriction fragment from pMON26461 and the 399 base pair SnaBI, HindIII restriction fragment from pMON3988, and the ligation reaction mixture was used to transform *E. coli*.

5 Transformant bacteria were selected on spectinomycin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The *E. coli* expression plasmid, pMON26472, encodes the fusion with the following amino
10 acid sequence:

Peptide # [SEQ ID NO:167]

DNA sequence # [SEQ ID NO:185] codes for the
15 foregoing pMON26472 polypeptide.

The gene encoding the fusion was transferred as a NcoI, HindIII fragment to the mammalian expression vector, pMON3934, and the resulting plasmid was designated pMON26474.

20 Various other examples will be apparent to the person skilled in the art after reading the present disclosure without departing from the spirit and scope of the invention. It is intended that all such other examples be included within the scope of the appended
25 claims.

AML Proliferation Assay for Bioactive Human Interleukin-3

The factor-dependent cell line AML 193 was obtained from the American Type Culture Collection (ATCC,
30 Rockville, MD). This cell line, established from a patient with acute myelogenous leukemia, is a growth factor dependent cell line which displayed enhanced growth in GM-CSF supplemented medium (Lange, B., et al., (1987); Valtieri, M., et al., (1987)). The ability of AML
35 193 cells to proliferate in the presence of human IL-3 has also been documented. (Santoli, D., et al., (1987)). A cell line variant was used, AML 193 1.3, which was adapted for long term growth in IL-3 by washing out the

growth factors and starving the cytokine dependent AML 193 cells for growth factors for 24 hours. The cells are then replated at 1×10^5 cells/well in a 24 well-plate in media containing 100 U/ml IL-3. It took approximately 2 months for the cells to grow rapidly in IL-3. These cells are maintained as AML 193 1.3 thereafter by supplementing tissue culture medium (see below) with human IL-3.

AML 193 1.3 cells are washed 6 times in cold Hanks balanced salt solution (HBSS, Gibco, Grand Island, NY) by centrifuging cell suspensions at $250 \times g$ for 10 minutes followed by decantation of the supernatant. Pelleted cells are resuspended in HBSS and the procedure is repeated until six wash cycles are completed. Cells washed six times by this procedure are resuspended in tissue culture medium at a density ranging from 2×10^5 to 5×10^5 viable cells/ml. This medium is prepared by supplementing Iscove's modified Dulbecco's Medium (IMDM, Hazelton, Lenexa, KS) with albumin, transferrin, lipids and 2-mercaptoethanol. Bovine albumin (Boehringer-Mannheim, Indianapolis, IN) is added at $500 \mu\text{g/ml}$; human transferrin (Boehringer-Mannheim, Indianapolis, IN) is added at $100 \mu\text{g/ml}$; soybean lipid (Boehringer-Mannheim, Indianapolis, IN) is added at $50 \mu\text{g/ml}$; and 2-mercaptoethanol (Sigma, St. Louis, MO) is added at $5 \times 10^{-5} \text{ M}$.

Serial dilutions of human interleukin-3 or fusion protein (hIL-3 mutein) are made in triplicate series in tissue culture medium supplemented as stated above in 96 well Costar 3596 tissue culture plates. Each well contained $50 \mu\text{l}$ of medium containing interleukin-3 or fusion protein once serial dilutions are completed. Control wells contained tissue culture medium alone (negative control). AML 193 1.3 cell suspensions prepared as above are added to each well by pipetting $50 \mu\text{l}$ (2.5×10^4 cells) into each well. Tissue culture plates are incubated at 37°C with 5% CO_2 in humidified

air for 3 days. On day 3, 0.5 μ Ci 3 H-thymidine (2 Ci/mM, New England Nuclear, Boston, MA) is added in 50 μ l of tissue culture medium. Cultures are incubated at 37°C with 5% CO₂ in humidified air for 18-24 hours. Cellular DNA is harvested onto glass filter mats (Pharmacia LKB, Gaithersburg, MD) using a TOMTEC cell harvester (TOMTEC, Orange, CT) which utilized a water wash cycle followed by a 70% ethanol wash cycle. Filter mats are allowed to air dry and then placed into sample bags to which scintillation fluid (Scintiverse II, Fisher Scientific, St. Louis, MO or BetaPlate Scintillation Fluid, Pharmacia LKB, Gaithersburg, MD) is added. Beta emissions of samples from individual tissue culture wells are counted in a LKB Betaplate model 1205 scintillation counter (Pharmacia LKB, Gaithersburg, MD) and data is expressed as counts per minute of 3 H-thymidine incorporated into cells from each tissue culture well. Activity of each human interleukin-3 preparation or fusion protein preparation is quantitated by measuring cell proliferation (3 H-thymidine incorporation) induced by graded concentrations of interleukin-3 or fusion protein. Typically, concentration ranges from 0.05 pM - 10⁵ pM are quantitated in these assays. Activity is determined by measuring the dose of interleukin-3 or fusion molecule which provides 50% of maximal proliferation [EC₅₀ = 0.5 x (maximum average counts per minute of 3 H-thymidine incorporated per well among triplicate cultures of all concentrations of interleukin-3 tested - background proliferation measured by 3 H-thymidine incorporation observed in triplicate cultures lacking interleukin-3)]. This EC₅₀ value is also equivalent to 1 unit of bioactivity. Every assay is performed with native interleukin-3 as a reference standard so that relative activity levels could be assigned.

Typically, the protein fusions were tested in a concentration range of 2000pM to 0.06pM titrated in serial 2 fold dilutions. Biological activity of the

fusion molecules was compared to the following standards as described below.

Protein fusions comprised in part of G-CSF, pMON3987, pMON3995, pMON3997, pMON26406, pMON26433, pMON26415, pMON26416, and pMON26430, were compared to the dose response curve of equal molar concentrations of hG-CSF and pMON13288 or pMON13416.

Protein fusions comprised in part of GM-CSF, pMON3989 and pMON3998 were compared to the dose response curve of equal molar concentrations of hGM-CSF and pMON13288.

Protein fusions comprised of dimers of hIL-3 variants, pMON3988, pMON26425, pMON26427, pMON26420, pMON26429 and pMON26431 were compared to the dose response curve of pMON13288 or pMON13416.

Activity for each sample was determined by the concentration which gave 50% of the maximal response by fitting a four-parameter logistic model to the data. It was observed that the upper plateau (maximal response) for the sample and the standard with which it was compared did not differ. Therefore relative potency calculation for each sample was determined from EC50 estimations for the sample and the standard as indicated above. Relative potency (EC50 of standard divided by EC50 of sample) reported in Table 3 is the mean of at least two independent assays unless indicated.

AML 193.1.3 cells proliferate in response to hIL-3, hGM-CSF and hG-CSF. Therefore the following additional assays were performed for some samples to demonstrate that the G-CSF or GM-CSF portion of the fusion proteins was active. Proliferation assay was performed using neutralizing polyclonal antibodies to pMON13288. In addition, a fusion molecule with the factor Xa cleavage site was cleaved then purified and the halves of the molecule were assayed for proliferative activity. These experiments showed that both components of the fusion protein were active.

Table 3 AML cell proliferation assay

pMON	R1	Linker	R2	AML 193.1.3 Bioactivity (relative potency)
pMON3987	13288	Linker 1	G-CSF	0.35 \pm 0.11
pMON3988	13288	Linker 1	13288	0.64 \pm 0.13
pMON3989	13288	Linker 1	GM-CSF	0.6 \pm 0.09
pMON3995	G-CSF	Linker 1	13288	0.41 \pm 0.44
pMON3997	13288	Linker 7	G-CSF	0.26 (n=1)
pMON3998	13288	Linker 7	GM-CSF	0.21 (n=1)
pMON26406	13288	Linker 4	G-CSF	0.37 \pm 0.30
pMON26433	G-CSF	Linker 4	13288	0.79 \pm 0.35
pMON26415	13288	Linker 1	G-CSF Ser17	0.46 \pm 0.08
pMON26416	G-CSF	Linker 1	13416	0.43 \pm 0.02
pMON26425	13288	Linker 2	13288	1.32 \pm 0.41
pMON26427	13288	Linker 3	13288	1.41 \pm 0.91
pMON26420	13416	Linker 1	13416	2.09 \pm 0.52
pMON26430	13288	Linker 6	G-CSF	1.04 \pm 0.69
pMON26429	13288	Linker 5	13288	1.88 \pm 0.09
pMON26431	13288	Linker 6	13288	0.66 \pm 0.26

Methylcellulose Assay

5 This assay provides a reasonable approximation of the growth activity of colony stimulating factors to stimulate normal bone marrow cells to produce different types of hematopoietic colonies in vitro (Bradley et al., 1966, Pluznik et al., 1965).

10 Methods

Approximately 30 ml of fresh, normal, healthy bone marrow aspirate are obtained from individuals. Under sterile conditions samples are diluted 1:5 with a 1X PBS (#14040.059 Life Technologies, Gaithersburg, MD.) solution in a 50 ml conical tube (#25339-50 Corning, Corning MD). Ficoll (Histopaque 1077 Sigma H-8889) is layered under the diluted sample and centrifuged, 300 x g for 30 min. The mononuclear cell band is removed and washed two times in 1X PBS and once with 1% BSA PBS (CellPro Co., Bothel, WA). Mononuclear cells are counted and CD34+ cells are selected using the Cephate LC (CD34) Kit (CellPro Co., Bothel, WA) column. This fractionation is performed since all stem and progenitor cells within the bone marrow display CD34 surface antigen.

25

Cultures are set up in triplicate with a final volume of 1.0 ml in a 35 X 10 mm petri dish (Nunc#174926).

Culture medium is purchased from Terry Fox Labs. (HCC-4230 medium (Terry Fox Labs, Vancouver, B.C., Canada) and erythropoietin (Amgen, Thousands Oaks, CA.) is added to the culture media. 3,000-10,000 CD34+ cells are added per dish. Native IL-3 and fusion molecules are added to give final concentrations ranging from .001nM 10nM.

Native IL-3 and fusion molecules are supplied in house.

35 G-CSF (Neupogen) is from Amgen.

Cultures are resuspended using a 3cc syringe and 1.0 ml is dispensed per dish. Control (baseline response)

cultures received no colony stimulating factors.

Positive control cultures received conditioned media (PHA stimulated human cells: Terry Fox Lab. H2400). Cultures are incubated at 37°C, 5% CO₂ in humidified air.

5 Hematopoietic colonies which are defined as greater than
10 50 cells are counted on the day of peak response (days 10-11) using a Nikon inverted phase microscope with a 40x objective combination. Groups of cells containing fewer than 50 cells are referred to as clusters. Alternatively colonies can be identified by spreading the colonies on a slide and stained or they can be picked, resuspended and spun onto cytopsin slides for staining.

Human Cord Blood Hemopoietic Growth Factor Assays

15

Bone marrow cells are traditionally used for in vitro assays of hematopoietic colony stimulating factor (CSF) activity. However, human bone marrow is not always available, and there is considerable variability between donors. Umbilical
20 cord blood is comparable to bone marrow as a source of hematopoietic stem cells and progenitors (Broxmeyer et al., 1992; Mayani et al., 1993). In contrast to bone marrow, cord blood is more readily available on a regular basis. There is also a potential to reduce assay variability by pooling cells
25 obtained fresh from several donors, or to create a bank of cryopreserved cells for this purpose. By modifying the culture conditions, and/or analyzing for lineage specific markers, it should be possible to assay specifically for granulocyte / macrophage colonies (CFU-GM), for megakaryocyte CSF activity, or
30 for high proliferative potential colony forming cell (HPP-CFC) activity.

Methods

Mononuclear cells (MNC) are isolated from cord blood within 24
35 hr. of collection, using a standard density gradient (1.077g/ml Histopaque). Cord blood MNC have been further enriched for stem cells and progenitors by several procedures, including

immunomagnetic selection for CD14-, CD34+ cells; panning for SBA-, CD34+ fraction using coated flasks from Applied Immune Science (Santa Clara, CA); and CD34+ selection using a CellPro (Bothell, WA) avidin column. Either freshly isolated or
5 cryopreserved CD34+ cell enriched fractions are used for the assay. Duplicate cultures for each serial dilution of sample (concentration range from 1pM to 1204pM) are prepared with 1×10^4 cells in 1ml of .9% methycellulose containing medium without additional growth factors (Methocult H4230 from Stem Cell
10 Technologies, Vancouver, BC.). In some experiments, Methocult H4330 containing erythropoietin (EPO) was used instead of Methocult H4230, or Stem Cell Factor (SCF), 50ng/ml (Biosource International, Camarillo, CA) was added. After culturing for 7-9 days, colonies containing >30 cells are counted. In order to
15 rule out subjective bias in scoring, assays are scored blind.

Analysis of c-mpl ligand proliferative activity

20

Methods

1. Bone marrow proliferation assay

a. CD34+ Cell Purification:

25 Between 15-20 ml bone marrow aspirates were obtained from normal allogeneic marrow donors after informed consent. Cells were diluted 1:3 in phosphate buffered saline (PBS, Gibco-BRL), 30 ml were layered over 15 ml Histopaque-1077 (Sigma) and centrifuged for 30 minutes at
30 300 RCF. The mononuclear interface layer was collected and washed in PBS. CD34+ cells were enriched from the mononuclear cell preparation using an affinity column per manufacturers instructions (CellPro, Inc, Bothell WA). After enrichment, the purity of CD34+ cells was 70% on
35 average as determined by using flow cytometric analysis using anti CD34 monoclonal antibody conjugated to fluorescein and anti CD38 conjugated to phycoerythrin (Becton Dickinson, San Jose CA).

Cells were resuspended at 40,000 cells/ml in X-Vivo 10 media (Bio-Whittaker, Walkersville, MD) and 1 ml was plated in 12-well tissue culture plates (Costar). The growth factor rhIL-3 was added at 100 ng/ml (pMON5873) was added to some wells. hIL3 variant, pMON13288, was used at 10 ng/ml or 100 ng/ml. Conditioned media from BHK cells transfected with plasmid encoding c-mpl ligand were tested by addition of 100 µl of supernatant added to 1 ml cultures (approximately a 10% dilution). Cells were incubated at 37°C for 8-14 days at 5% CO₂ in a 37°C humidified incubator.

b. Cell Harvest and Analysis:

At the end of the culture period a total cell count was obtained for each condition. For fluorescence analysis and ploidy determination cells were washed in megakaryocyte buffer (MK buffer, 13.6 mM Sodium Citrate, 1 mM Theophylline, 2.2 µM PGE₁, 11 mM Glucose, 3% w/v BSA, in PBS, pH 7.4,) [Tomer et al., (1987)] resuspended in 500 µl of MK buffer containing anti-CD41a FITC antibody (1:200, AMAC, Westbrook, ME) and washed in MK buffer. For DNA analysis cells were permeablized in MK buffer containing 0.5% Tween 20 (Fisher, Fair Lawn NJ) for 20 min. on ice followed by fixation in 0.5% Tween-20 and 1% paraformaldehyde (Fisher Chemical) for 30 minutes followed by incubation in Propidium Iodide (Calbiochem, La Jolla Ca) (50 µg/ml) with RNA-ase (400 U/ml) in 55% v/v MK buffer (200mOsm) for 1-2 hours on ice. Cells were analyzed on a FACScan or Vantage flow cytometer (Becton Dickinson, San Jose, CA). Green fluorescence (CD41a-FITC) was collected along with linear and log signals for red fluorescence (PI) to determine DNA ploidy. All cells were collected to determine the percent of cells that were CD41+. Data analysis was performed using software by LYSIS (Becton Dickinson, San Jose, CA). Percent of cells expressing the CD41 antigen was obtained from flow cytometry analysis (Percent). Absolute (Abs) number of

150

CD41+ cells/ml was calculated by: $(\text{Abs}) = (\text{Cell Count}) * (\text{Percent}) / 100$.

2. Megakaryocyte fibrin clot assay.

5

CD34+ enriched population were isolated as described above. Cells were suspended at 25,000 cells/ml with/without cytokine(s) in a media consisting of a base Iscoves IMDM media supplemented with 0.3% BSA, 0.4mg/ml apo-transferrin, 6.67 μ M FeCl₂, 25 μ g/ml CaCl₂, 25 μ g/ml L-asparagine, 500 μ g/ml E-amino-n-caproic acid and Penicillin/Streptomycin. Prior to plating into 35mm plates, thrombin was added (0.25 Units/ml) to initiate clot formation. Cells were incubated at 37°C for 13 days at 5% CO₂ in a 37°C humidified incubator.

At the end of the culture period plates were fixed with Methanol:Acetone (1:3), air dried and stored at -200C until staining. A peroxidase immunocytochemistry staining procedure was used (Zymed, Histostain-SP. San Francisco, CA) using a cocktail of primary monoclonal antibodies consisting of anti CD41a, CD42 and CD61. Colonies were counted after staining and classified as negative, CFU-MK (small colonies, 1-2 foci and less than approx. 25 cells), BFU-MK (large, multi-foci colonies with > 25 cells) or mixed colonies (mixture of both positive and negative cells).

Example 70

30 Administration of hIL-3 variant, pMON13288, and c-mpl ligand fusion molecule has a more than additive effect on megakaryocyte expansion than either cytokine alone.

Megakaryocyte fibrin clot cultures were set up as described in methods section. pMON26448 is the 1-153 amino acid form of c-mpl ligand (Meg-CSF). pMON26463 is a fusion molecule consisting of hIL3 variant, pMON13288

and the 1-153 amino acid form of c-mpl ligand.

Incubation in the presence of hIL3 variant, pMON13288 gave rise to colonies that were predominantly negative for megakaryocyte markers (86/114, (Table 4)) except for

5 number of small CFU-MK colonies (23/114). pMON26448 alone gave rise primarily to CFU-MK colonies (172/175) with only a few number of negative colonies (3/175).

Combination of hIL3 variant, pMON13288 and pMON26448 gave rise to a large number of positive colonies (295/414)

10 that were predominantly of the BFU-MK morphology. There were a negative colonies as well (119/414). Total number of positive colonies with co-administration was more than additive than with either cytokine alone. pMON26463, the fusion molecule gave results similar to the combination

15 of hIL3 variant, pMON13288 and pMON26448. The number of negative cells is less than with hIL3 variant, pMON13288 which is probably due to a lower concentration of pMON13288 in the preparation (approximately 10ng/ml as part of the fusion molecule vs. 100ng/ml of hIL3 variant.

20 pMON13288)

Table 4.

cytokine treatment	Colonies/Well				
	Negative	CFU-MK	BFU-MK	Mixed	Total
pMON13288	86	23	0	5	114
pMON26448	3	73	98	1	175
pMON26448 + pMON13288	119	29	244	22	414
pMON26463	10	30	165	17	222
cytokine treatment	Colonies/100,000 plated				
	Negative	CFU-MK	BFU-MK	Mixed	Total
pMON13288	344	92	0	20	456
pMON26448	12	292	392	4	700
pMON26448 + pMON13288	476	116	976	88	1656

152

pMON26463	40	120	660	68	888
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IL-3 Mediated Sulfidoleukotriene Release from Human Mononuclear Cells

The following assay is used to measure IL-3 mediated
5 sulfidoleukotriene release from human mononuclear cells.

Heparin-containing human blood is collected and layered
onto an equal volume of Ficoll-Paque (Pharmacia # 17-
0840-02) ready to use medium (density 1.077 g/ml.). The
10 Ficoll is warmed to room temperature prior to use and
clear 50 ml polystyrene tubes are utilized. The Ficoll
gradient is spun at 300 x g for 30 minutes at room
temperature using a H1000B rotor in a Sorvall RT6000B
refrigerated centrifuge. The band containing the
15 mononuclear cells is carefully removed, the volume
adjusted to 50 mls with Dulbecco's phosphate-buffered
saline (Gibco Laboratories cat. # 310-4040PK), spun at
400 x g for 10 minutes at 4°C and the supernatant is
carefully removed. The cell pellet is washed twice with
20 HA Buffer [20 mM Hepes (Sigma # H-3375), 125 mM NaCl
(Fisher # S271-500), 5 mM KCl (Sigma # P-9541), 0.5 mM
glucose (Sigma # G-5000), 0.025% Human Serum Albumin
(Calbiochem # 126654) and spun at 300 x g, 10 min., 4°C.
The cells are resuspended in HACM Buffer (HA buffer
25 supplemented with 1 mM CaCl₂ (Fisher # C79-500) and 1 mM
MgCl₂ (Fisher # M-33) at a concentration of 1 x 10⁶
cells/ml and 180 µl are transferred into each well of 96
well tissue culture plates. The cells are allowed to
acclimate at 37°C for 15 minutes. The cells are primed by
30 adding 10 µls of a 20 X stock of various concentrations
of cytokine to each well (typically 100000, 20000, 4000,
800, 160, 32, 6.4, 1.28, 0 fM IL3). The cells are
incubated for 15 minutes at 37°C. Sulfidoleukotriene
release is activated by the addition of 10 µls of 20 X
35 (1000 nM) fmet-leu-phe (Calbiochem # 344252) final
concentration 50nM FMLP and incubated for 10 minutes at

153

- 37°C. The plates are spun at 350 x g at 4°C for 20 minutes. The supernatants are removed and assayed for sulfidoleukotrienes using Cayman's Leukotriene C4 EIA kit (Cat. #420211) according to manufacturers' directions.
- 5 Native hIL-3 is run as a standard control in each assay.

- Further details known to those skilled in the art may be found in T. Maniatis, et al. Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory (1982)
- 10 and references cited therein, incorporated herein by reference; and in J. Sambrook, et al., Molecular Cloning, A Laboratory Manual, 2nd edition, Cold Spring Harbor Laboratory (1989) and references cited therein, incorporated herein by reference.

- 15 Additional details on the IL-3 variants of the present invention may be found in co-pending United States Patent Application Serial number PCT/US93/11197 which is hereby incorporated by reference in its
- 20 entirety as if written herein.

Additional details on how to make the fusion protein can be found in WO 92/04455 and WO 91/02754.

- 25 Additional details about the lymphokine and the variants thereof can be found in U.S. Patent 4,810,643, and 5,218,092 E.P. Application 02174004.

All references, patents or applications cited herein are incorporated by reference in their entirety as if written herein.

- 30 Amino acids are shown herein by standard one letter or three letter abbreviations as follows:

35	Abbreviated Designation	Amino Acid
	A Ala	Alanine
	C Cys	Cysteine
	D Asp	Aspartic acid

154

	E	Glu	Glutamic acid
	F	Phe	Phenylalanine
	G	Gly	Glycine
	H	His	Histidine
5	I	Ile	Isoleucine
	K	Lys	Lysine
	L	Leu	Leucine
	M	Met	Methionine
	N	Asn	Asparagine
10	P	Pro	Proline
	Q	Gln	Glutamine
	R	Arg	Arginine
	S	Ser	Serine
	T	Thr	Threonine
15	V	Val	Valine
	W	Trp	Tryptophan
	Y	Tyr	Tyrosine

20

TABLE 5 OLIGONUCLEOTIDES

25	88CTERM1.REQ	Length: 000041
	AATTCGGGA AAAACTGACG TTCTATCTGG TTACCCTTGA G [SEQ ID NO:91]	
	88CTERM4.REQ	Length: 000046
30	CTGCGCTTGC TCAAGGGTAA CCAGATAGAA CGTCAGTTTT TCCCGG [SEQ ID NO:92]	
	88XA2.REQ	Length: 000039
35	CAAGCGCAGG AACAACAGTA CGTAATCGAG GGAAGGATT [SEQ ID NO:93]	
	88XA5.REQ	Length: 000039
40	ACCCGGGGAA ATCCTTCCCT CGATTACGTA CTGTTGTTT [SEQ ID NO:94]	
	GLYN3.REQ	Length: 000063
	TCCCCGGGTG GTGTTCTGG CGGCGGCTCC AACATGTAAG GTACCGCATG CAAGCTTAGA TCT [SEQ ID NO:95]	
45	GLYN6.REQ	Length: 000058

155

AGCTAGATCT AAGCTTGCAT GCGGTACCTT ACATGTTGGA GCGGCCGCCA
GAACCACC [SEQ ID NO:96]

5 IGG2B1.REQ Length: 000074

CCGGGTGAAC CGTCTGGTCC AATCTCTACT ATCAACCCGT CTCTCCGTC
TAAAGAATCT CATAAATCTC CAAA [SEQ ID NO:97]

10 IGG2B2.REQ Length: 000074

CATGTTTGGA GATTATGAG ATTCTTTAGA CGGAGGAGAC GGGTTGATAG
TAGAGATTGG ACCAGACGGT TCAC [SEQ ID NO:98]

15 GCSFSNA1.REQ Length: 000068

CTAGCCATCT GCAGAGCTTC CTGGAGGTGT CGTACCGCGT TCTACGCCAC
CTTGCGCAGC CCTACGTA [SEQ ID NO:99]

20 GCSFSNA2.REQ Length: 000068

AGCTTACGTA GGGCTGCGCA AGGTGGCGTA GAACGCGGTA CGACACCTCC
AGGAAGCTCT GCAGATGG [SEQ ID NO:100]

25 LYSXA1.REQ Length: 000021

GTAATCGAGG GAAAGATTTC C [SEQ ID NO:101]

LYSXA2.REQ Length: 000025

30 CCGGGGAAAT CTTTCCCTCG ATTAC [SEQ ID NO:102]

GLYXA1.REQ Length: 000021

35 GTAGAGGGCG GTGGAGGCTC C [SEQ ID NO:103]

GLYXA2.REQ Length: 000025

CCGGGGAGCC TCCACGCCC TCTAC [SEQ ID NO:104]

40 GM-AUP.REQ Length: 000058

CATGGCACCA GCAAGATCAC CATCACCATC AACTCAACCT TGGGAACATG
TGAATGCC [SEQ ID NO:105]

45 GM-ALOW.REQ Length: 000052

CATTACATG TTCCCAAGGT TGAGTTGATG GTGATGGTGA TCTTGCTGGT
GC [SEQ ID NO:106]

50 G-CYS18.REQ Length: 000066

CTGCCAGCTC CCTGCCCCAG AGCTTCCTGC TCAAGTCTTT AGAGCAAGTG
AGGAAGATCC AGGGCG [SEQ ID NO:107]

55 GCYS18LO.REQ Length: 000066

CTGGATCTTC CTCATTGCT CTAAAGACTT GAGCAGGAAG CTCTGGGGCA
GGGAGCTGGC AGGGCC [SEQ ID NO:108]

60 HIL6231.REQ Length: 000048

156

AGCTTACCTG CCATGGGCTCC AGTACCACCA GGTGAAGATT CCAAAGAT
[SEQ ID NO:109]

5 HIL6232.REQ Length: 000040

TTGGAATCTT CACCTGGTGG TACTGGAGCC ATGGCAGGTA [SEQ ID NO:110]

10 HGCSFMA1.REQ Length: 000026

AGCTTCCATG GCTACCCCCC TGGGCC [SEQ ID NO:111]

HGCSFMA2.REQ Length: 000018

15 CAGGGGGGTA GCCATGGA [SEQ ID NO:112]

HGCSFAT1.REQ Length: 000020

20 CATGGCTACA CCATTGGGCC [SEQ ID NO:113]

HGCSFAT2.REQ Length: 000012

CAATGGTGTA GC [SEQ ID NO:114]

25 HGCSFAT3.REQ Length: 000020

CATGGCTACA CCATTAGGAC [SEQ ID NO:115]

30 HGCSFAT4.REQ Length: 000012

TAATGGTGTA GC [SEQ ID NO:116]

PREFOR.REQ

35 CCTGTCAACC CGGGCGGCGG CTCTGGTGGT [SEQ ID NO:117]

REVPRE.REQ

40 TCATAATACA TGTTACCGGA ACGGAGCCGC C [SEQ ID NO:118]

FORXTRA.REQ

ATCGTCTGAC CTCGGGGAC CTCCTGTCAA TGCT [SEQ ID NO:119]

45 XTRAREV.REQ

AGCGTTTGAC ATGTTTTTCAT AATCAAAATC [SEQ ID NO:120]

c-mplNcoI

50 ACGTCCATGGCNTCNCNCNCNCCTGCTTGTGACCTCCGAGTC [SEQ ID NO:169
(where N= G, C, T or A)]

c-mplEcoRI

55 AATAGCTGAATTCTTACCCTTCCTGAGACAGATT [SEQ ID NO:170]

c-mplHindIII

60 TGACAAGCTTACCTGACGCAGAGGGTGGACCCT [SEQ ID NO:171]

157

Eco-mp1

5

ATGCACGAATTCTCTGACGCAGAGGGTGGG [SEQ ID NO:172]

EcoSna1

AATTCCATGCATAC [SEQ ID NO:173]

10

ECOSNA2

GGTACGTATG [SEQ ID NO:174]

15

TABLE 6DNA SEQUENCES

pMON13023

20

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG

ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG

ATATCCTGAT GGAACGAAAC CTTGGAAGTC CAAACCTGCT CGCATTCGTA

25

AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG

TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC

30

CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGA AAACTGAGG

TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA

GGGAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA

35

CACCATTAGG CCCTGCCAGC TCCCTGCCCC AGAGCTTCCT GCTCAAGTGC

TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA

40

GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG

GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG

GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT

45

CTACCAGGGG CTCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC

CCACCTTGA CACACTGCAG CTGGACGTCG CCGACTTTGC CACCACCATC

50

TAACTGGGAA TGGSCCCTGC CCTGCAGCCC ACCCAGGGTG CCATGCCGGC

CTTCGCCTCT GCTTTCCAGC GCCGGGCAGG AGGGGTCTCT GTTGCTAGCC

ATCTGCAGAG CTTCCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGCG

55

CAGCCC [SEQ ID NO:53]

pMON13021

158

5 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTTCGTA
10 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
15 GGAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
ACTGCTCTAT AATGATCGAT GAAATTATAC ATCACTTAAA GAGACCACCT
AACCCTTTGC TGGACCCGAA CAACCTCAAT TCTGAAGACA TGGATATCCT
20 GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTG GTAAGGGCTG
TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC
25 CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT
CATCAAGGCA GGTGACTGGC AAGAATTCCG GGAAAACTG ACGTTCTATC
TGTTACCCT TGAGCAAGCG CAGGAACAAC AG [SEQ ID NO:54]
30

pMON13022

35 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
40 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTTCGTA
AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
45 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCAC
50 CGGCTCGTTC CCCGTCCCCG TCTACCCAGC CGTGGGAACA CGTGAATGCC
ATCCAGGAGG CCCGGCGTCT CCTGAACCTG AGTAGAGACA CTGCTGCTGA
55 GATGAATGAA ACAGTAGAAG TGATATCAGA AATGTTTGAC CTCCAGGAGC
CGACTTGCCT ACAGACCCGC CTGGAGCTGT ACAAGCAGGG CCTGCGGGGC
60 AGCCTCACCA AGCTCAAGGG CCCCTTGACC ATGATGGCCA GCCACTACAA

159

GCAGGACTGC CCTCCAACCC CGGAAACTTC CTGTGCAACC CAGATTATCA
CCTTGGAAAG TTTCAAAGAG AACCTGAAGG ACTTCCTGCT TGTGATCCCC
5 TTTGACTGCT GGGAGCCAGT CCAGGAG [SEQ ID NO:55]

pMON13039

10 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACTTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
15 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGCTA
AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
20 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
25 CACCATTGGG CCCTGCCAGC TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT
TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA
GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG
30 GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG
GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT
35 CTACCAGGGG CTCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC
CCACCTTGA CACACTGCAG CTGGACGTCG CCGACTTTGC CACCACCATC
40 TGGCAGCAGA TGGAAGAACT GGAATGGCC CCTGCCCTGC AGCCACCCA
GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG GCAGGAGGGG
45 TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT
CTACGCCACC TTGCGCAGCC C [SEQ ID NO:56]

pMON13049

50 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACTTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
55 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGCTA
AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
60 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC

160

CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
5 GGGAAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTC
CAGTACCACC AGGTGAAGAT TCCAAAGATG TGGCCGCCCC ACACAGACAG
CCACTCACCT CTTCAGAACG AATTGACAAA CAAATTCGGT ACATCCTCGA
10 CGGGATATCA GCCCTGAGAA AGGAGACATG TAACAAGAGT AACATGTGTG
AAAGCAGCAA AGAGGCGCTA GCAGAAAACA ACCTGAACCT TCCAAAGATG
15 GCTGAAAAAG ATGGATGCTT CCAATCCGGA TTCAATGAGG AGACTTGCCT
GGTGAANAATC ATCACTGGTC TTTTGGAGTT TGAGGTATAC CTCGAGTACC
TCCAGAACAG ATTTGAGAGT AGTGAGGAAC AAGCCAGAGC TGTGCAGATG
20 TCGACAAAAG TCCTGATCCA GTTCCTGCAG AAAAAGGCAA AGAATCTAGA
TGCAATAACC ACCCCTGACC CAACCACAAA TGCATCCCTG CTGACGAAGC
25 TGCAGGCACA GAACCACTGG CTGCAGGACA TGACAACTCA TCTCATTCTG
CGCAGCTTTA AGGAGTTCCT GCAGTCCAGC CTGAGGGCTC TTCGGCAAAT
G [SEQ ID NO:57]

pMON13055

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
35 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCTGT
40 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
45 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAAGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
50 ACTGCTCTAT AATGATCGAT GAAATTATAC ATCACTTAAA GAGACCACCT
AACCCTTTGC TGGACCCGAA CAACCTCAAT TCTGAAGACA TGGATATCCT
GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTG GTAAGGGCTG
55 TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC
CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT
60 CATCAAGGCA GGTGACTGGC AAGAATTCCG GGAAAACTG ACGTTCTATC

TGGTTACCCCT TGAGCAAGCG CAGGAACAAC AG [SEQ ID NO:58]

5 PMON13054

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTGGAATC CAAACCTGCT CGCATTGCTA
AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAAGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
CACCATTGGG CCCTGCCAGC TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT
TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA
GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG
GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG
GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT
CTACCAGGGG CTCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC
CCACCTTGA CACACTGCAG CTGGACGTCG CCGACTTTGC CACCACCATC
TGGCAGCAGA TGGAAGAACT GGAATGGCC CCTGCCCTGC AGCCACCCCA
GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG GCAGGAGGGG
TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT
CTACGCCACC TTGCGCAGCC C [SEQ ID NO:59]

45

PMON13056

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTGGAATC CAAACCTGCT CGCATTGCTA
AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG

60

162

TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
CGGTGGAGGC TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
5 CACCATTGGG CCCTGCCAGC TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT
TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA
10 GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG
GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG
GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCATAGCG GCCTTTTCCT
15 CTACCAGGGG CTCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGGTC
CCACCTTGA CACTGCAG CTGGACGTC CCGACTTTC CACCACCATC
TGGCAGCAGA TGGAAGAACT GGAATGGCC CCTGCCCTGC AGCCACCCA
20 GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG GCAGGAGGGG
TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT
25 CTACGCCACC TTGCGCAGCC C [SEQ ID NO:60]

PMON13057

30 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
35 ATATCCTGAT GGAACGAAAC CTTGGAATC CAAACCTGCT CGCATTTCGTA
AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
40 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
45 CGGTGGAGGC TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
ACTGCTCTAT AATGATCGAT GAAATTATAC ATCACTTAAA GAGACCACCT
AACCCTTTC TGGACCCGAA CAACCTCAAT TCTGAAGACA TGGATATCCT
50 GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGATTTC GTAAGGGCTG
TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC
CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT
55 CATCAAGGCA GGTGACTGGC AAGAATTCCG GGAAAACTG ACGTTCTATC
TGTTACCCT TGAGCAAGCG CAGGAACAAC AG [SEQ ID NO:61]

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163

pMON13036

5 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCGTA
10 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
15 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTAACTGC
20 TCTATAATGA TCGATGAAAT TATACATCAC TTAAAGAGAC CACCTAACCC
TTTGCTGGAC CCGAACAACC TCAATTCTGA AGACATGGAT ATCCTGATGG
25 AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG
CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCAACC
ATGTCTGCCC TCTGCCACGG CCGCACCCCTC TCGACATCCA ATCATCATCA
30 AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA AACTGACGTT CTATCTGGTT
ACCCTTGAGC AAGCGCAGGA ACAACAG [SEQ ID NO:62]

35

pMON13059

40 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCGTA
45 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
50 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTAACTGC
55 TCTATAATGA TCGATGAAAT TATACATCAC TTAAAGAGAC CACCTAACCC
TTTGCTGGAC CCGAACAACC TCAATTCTGA AGACATGGAT ATCCTGATGG
60 AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG

164

5 CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC
ATGTCTGCCC TCTGCCACGG CCGCACCCCTC TCGACATCCA ATCATCATCA
AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA AACTGACGTT CTATCTGGTT
ACCCTTGAGC AAGCGCAGGA ACAACAG [SEQ ID NO:63]

10

pMON13061

15 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCGTA
20 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACC
25 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
CGGTGGAGGC TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTAACTGC
30 TCTATAATGA TCGATGAAAT TATACATCAC TTAAAGAGAC CACCTAACCC
TTTGCTGGAC CCGAACAACC TCAATTCTGA AGACATGGAT ATCCTGATGG
35 AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGCGTAAG GGCTGTCAAG
CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC
ATGTCTGCCC TCTGCCACGG CCGCACCCCTC TCGACATCCA ATCATCATCA
40 AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA AACTGACGTT CTATCTGGTT
ACCCTTGAGC AAGCGCAGGA ACAACAG [SEQ ID NO:64]

45

pMON13062

50 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCGTA
55 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACC
60 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA

165

5 GGAAGGATT TCCCCCGGGC CTCCTGTCAA TGCTGGCGGC GGCTCTGGTG
GTGGTTCTGG TGGCGGCTCT GAGG3TGGCG GCTCTGAGG3 TGGCGGTTCT
GAGGGTGGCG GCTCTGAGG3 TGGCGGTTCC GGTGGCGGCT CCGGTTCCGG
TGATTTTGAT TATGAAAACA TGGCTACACC ATTGGGCCCT GCCAGCTCCC
10 TGCCCCAGAG CTTCTGCTC AAGTCTTTAG AGCAAGTGAG GAAGATCCAG
GGCGATGGCG CAGCGCTCCA GGAGAAGCTG TGTGCCACCT ACAAGCTGTG
15 CCACCCCGAG GAGCTGGTGC TGCTCGGACA CTCTCTGGGC ATCCCCTGGG
CTCCCCTGAG CTCCTGCCCC AGCCAGGCCC TGCAGCTGGC AGGCTGCTTG
AGCCAACTCC ATAGCGGCCT TTTCTCTAC CAGGGGCTCC TGCAGGCCCT
20 GGAAGGGATA TCCCCCGAGT TGGGTCCCAC CTTGGACACA CTGCAGCTGG
ACGTCGCCGA CTTTGCCACC ACCATCTGGC AGCAGATGGA AGAACTGGGA
ATGGCCCCCTG CCCTGCAGCC CACCCAGGGT GCCATGCCGG CTTTCGCCCTC
25 TGCTTTCCAG CGCCGGGCAG GAGGGTCTCT GGTGCTAGC CATCTGCAGA
GCTTCCTGGA GGTGTCGTAC CGCGTTCTAC GCCACCTTGC GCAGCCC
30 [SEQ ID NO: 65]

PMON13031

35 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTGGAATC CAAACCTGCT CGCATTCGTA
40 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
45 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGAAGGATT TCCCCCGGGC CTCCTGTCAA TGCTGGCGGC GGCTCTGGTG
50 GTGGTTCTGG TGGCGGCTCT GAGG3TGGCG GCTCTGAGGG TGGCGGTTCT
GAGGGTGGCG GCTCTGAGGG TGGCGGTTCC GGTGGCGGCT CCGGTTCCGG
TGATTTTGAT TATGAAAACA TGGCACCAGG TCGTTCCCCG TCCCCGTCTA
55 CCCAGCCGTG GGAACACGTG AATGCCATCC AGGAGGCCCC GCGTCTCCTG
AACCTGAGTA GAGACACTGC TGCTGAGATG AATGAAACAG TAGAAGTGAT
60 ATCAGAAATG TTTGACCTCC AGGAGCCGAC TTGCCTACAG ACCCGCCTGG

166

AGCTGTACAA GCAGGGCCTG CGGGGCAGCC TCACCAAGCT CAAGGGGCCCC
TTGACCATGA TGGCCAGCCA CTACAAGCAG CACTGCCCTC CAACCCCGGA
5 AACTTCCTGT GCAACCCAGA TTATCACCTT TGAAAGTTTC AAAGAGAACC
TGAAGGACTT CCTGCTTGTC ATCCCCTTTG ACTGCTGGGA GCCAGTCCAG
10 GAG [SEQ ID NO:66]

PMON15937

15 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCTGTA
20 AGGGCTCTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
25 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGAAGGATT TCCCCCGGTG GCGGCGGCTC TGGTGGTGGT TCTGGTGGCG
30 GCTCTGAGGG TGGCGGCTCT GAGGGTGGCG GTTCTGAGGG TGGCGGCTCT
GAGGGTGGCG GTTCCGGTGG CGGCTCCGGT TCCGGTAACA TGGCTACACC
ATTAGGCCCT GCCAGCTCCC TGCCCCAGAG CTTCTGCTC AAGTGCTTAG
35 AGCAAGTGAG GAAGATCCAG GGCGATGGCG CAGCGCTCCA GGAGAAGCTG
TGTGCCACCT ACAAGCTGTG CCACCCCGAG GAGCTGGTGC TGCTCGGACA
40 CTCTCTGGG ATCCCCTGGG CTCCCCTGAG CTCCTGCCCC AGCCAGGCCC
TGCAGCTGGC AGGCTGCTTG AGCCAACTCC ATAGCGGCCT TTTCTCTAC
CAGGGGCTCC TGCAGGCCCT GGAAGGGATA TCCCCGAGT TGGGTCCAC
45 CTTGGACACA CTGCAGCTGG ACGTCGCCGA CTTTGCCACC ACCATCTGGC
AGCAGATGGA AGAACTGGGA ATGGCCCCTG CCCTGCAGCC CACCCAGGGT
50 GCCATGCCGG CCTTCGCCTC TGCTTTCCAG CGCCGGGCAG GAGGGTCTCT
GGTTGCTAGC CATCTGCAGA GCTTCCTGGA GGTGTCGTAC CGCGTTCTAC
55 GCCACCTTGC GCAGCCC [SEQ ID NO:67]

PMON13034

60 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG

167

ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTTCGTA
5 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
10 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
15 CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTACACCA
TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC TTCCTGCTCA AGTGCTTAGA
GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG GAGAAGCTGT
20 GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC
TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT
25 GCAGCTGGCA GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCTCTACC
AGGGGCTCCT GCAGGCCCTG GCTGGATAT CCCCCGAGTT GGGTCCCACC
TTGGACACAC TGCAGCTGGA CACCCGAC TTTGCCACCA CCATCTGGCA
30 GCAGATGGAA GAACTGGGAA TGGCCCTGTC CCTGCAGCCC ACCCAGGGTG
CCATGCCGGC CTTCGCCTCT GCTTCCAGC GCCGGGCAGG AGGGGTCTCTG
35 GTTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGTCGTACC GCGTTCTACG
CCACCTTGCG CAGCCC [SEQ ID NO:68]

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PMON13035

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
45 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTTCGTA
AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
50 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
55 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCAAACAT GGCACCGGCT
60

168

CGTTCCCCGT CCCCCTCTAC CCAGCCGTGG GAACACGTGA ATGCCATCCA
GGAGGCCCCG CGTCTCCTGA ACCTGAGTAG AGACACTGCT GCTGAGATGA
5 ATGAAACAGT AGAAGTGATA TCAGAAATGT TTGACCTCCA GGAGCCGACT
TGCCTACAGA CCCGCCTGGA GCTGTACAAG CAGGGCCTGC GGGGAGCCT
CACCAAGCTC AAGGGCCCCCT TGACCATGAT GGCCAGCCAC TACAAGCAGC
10 ACTGCCCTCC AACCCCGGAA ACTTCCTGTG CAACCCAGAT TATCACCTTT
GAAAGTTTCA AAGAGAACCT GAAGGACTTC CTGCTTGTCA TCCCCTTTGA
15 CTGCTGGGAG CCAGTCCAGG AG [SEQ ID NO:69]

PMON13058

20 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTGGAATC CAAACCTGCT CGCATTCGTA
25 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
30 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAAGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
35 CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTACACCA
TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC TTCTGTCTCA AGTGCTTAGA
40 GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG GAGAAGCTGT
GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC
TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCTGCCCCA GCCAGGCCCT
45 GCAGCTGGCA GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC
AGGGGCTCCT GCAGGCCCTG GAAGGGATAT CCCCCGAGTT GGGTCCCACC
50 TTGGACACAC TGCAGCTGGA CGTCGCCGAC TTTGCCACCA CCATCTGGCA
GCAGATGGAA GAACTGGGAA TGGCCCCCTGC CCTGCAGCCC ACCCAGGGTG
CCATGCCGGC CTTGCGCTCT GCTTTCAGC GCCGGGCAGG AGGGGTCTCG
55 GTTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGTGCTACC GCGTTCTACG
CCACCTTGCG CAGCCC [SEQ ID NO:70]

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PMON13060

5 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCGTA
10 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC COTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT CATGGCAAG AATTCCGGGA AAAACTGACG
15 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
CGGTGGAGGC TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
20 CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTACACCA
TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC TTCCTGCTCA AGTGCTTAGA
GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG GAGAAGCTGT
25 GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC
TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT
30 GCAGCTGGCA GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC
AGGGGCTCCT GCAGGCCCTG GAAGGGATAT CCCCCGAGTT GGGTCCCACC
TTGGACACAC TGCAGCTGGA CGTCGCCGAC TTTGCCACCA CCATCTGGCA
35 GCAGATGGAA GAACTGGGAA TGGCCCCCTGC CCTGCAGCCC ACCCAGGGTG
CCATGCCGGC CTTGCGCTCT GCTTTCAGC GCCGGGCAGG AGGGGTCTCG
40 GTTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGTCGTACC GCGTTCTACG
CGACCTTGCG CAGCCC [SEQ ID NO:71]

45

PMON13026

ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCTGTCT
50 CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
55 CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
TTTTCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCGAG
60 TTGGGTCCCA CTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC

170

5 CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCCCT GCCCTGCAGC
CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
GGAGGGSTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
10 CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATTT
CCCCGGSTGG TGGTTCTGGC GGCGGCTCCA ACATGGCTAA CTGCTCTATA
ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTA ACCCTTTGCT
15 GGACCCGAAC AACCTCAATT CTGAAGACAT GGATATCCTG ATGGAACGAA
ACCTTCGAAC TCCAAACCTG CTCGCATTCTG TAAGGGCTGT CAAGCACTTA
GAAAATGCAT CAGGTATTGA GGCAATTCTT CGTAATCTCC AACCATGTCT
20 GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC ATCAAGGCAG
GTGACTGGCA AGAATTCCGG GAAAACTGA CGTTCTATCT GGTTACCCTT
GAGCAAGCGC AGGAACAACA G [SEQ ID NO:72]

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PMON13063

30 ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
35 CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
TTTTCTCTA CCAGGGGCTC CTGCAGGCC TGAAGGGAT ATCCCCGAG
40 TTGGGTCCA CCTTGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCCCT GCCCTGCAGC
45 CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATTT
50 CCCCCGTGA ACGTCTGGT CCAATCTCTA CTATCAACCC GTCTCTCCG
TCTAAAGAAT CTCATAAATC TCCAAACATG GCTAACTGCT CTATAATGAT
55 CGATGAAATT ATACATCACT TAAAGAGACC ACCTAACCTT TTGCTGGACC
CGAACAACTT CAATTCTGAA GACATGGATA TCCTGATGGA ACGAAACCTT
CGAACTCCAA ACCTGCTCGC ATTGTAAGG GCTGTCAAGC ACTTAGAAAA
60

171

5 TGCATCAGGT ATTGAGGCAA TTCTTCGTAA TCTCCAACCA TGTCTGCCCT
CTGCCACGGC CGCACCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC
TGGCAAGAAT TCCGGGAAAA ACTGACGTTT TATCTGGTTA CCCTTGAGCA
AGCGCAGGAA CAACAG [SEQ ID NO:73]

10 PMON13064

15 ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
20 CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGGGAAGGGAT ATCCCCCGAG
25 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GAGCTCGCCG ACTTTGCCAC
CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCCCT GCCCTGCAGC
CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
30 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATTT
35 CCCCCGGGCC TCCTGTCAAT GCTGGCGGCG GCTCTGGTGG TGGTTCTGGT
GGCGGCTCTG AGGGTGGCGG CTCTGAGGGT GGCGGTTCTG AGGGTGGCGG
CTCTGAGGGT GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT GATTTTGATT
40 ATGAAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC
TTAAAGAGAC CACCTAACCC TTTGCTGGAC CCGAACAACC TCAATTCTGA
AGACATGGAT ATCCTGATGG AACGAAACCT TCGAACTCCA AACCTGCTCG
45 CATTCGTAAG GGCTGTCAAG CACTTAGAAA ATGCATCAGG TATTGAGGCA
ATTCTTCGTA ATCTCCAACC ATGTCTGCCC TCTGCCACGG CCGCACCTC
50 TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA
AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG
[SEQ ID NO:74]

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PMON13043

60 ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC

172

AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
5 CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
TTTTCTCTA CCAGGGGCTC CTGCAGGCCC TGGAAGGGAT ATCCCCCGAG
10 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC
CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
15 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATTT
20 CCCC GGGTGG TGGTTCTGGC GCGGCTCCA ACATGGCTAA CTGCTCTATA
ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTG CACCTTTGCT
GGACCCGAAC AACCTCAATG ACGAAGACGT CTCTATCCTG ATGGAACGAA
25 ACCTTCGACT TCCAAACCTG GAGAGCTTCG TAAGGGCTGT CAAGAACTTA
GAAAATGCAT CAGGTATTGA GGCAATTCTT CGTAATCTCC AACCATGTCT
30 GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC ATCAAGGCAG
GTGACTGGCA AGAATTCCGG GAAAACTGA CGTTCTATCT GGTACCCTT
35 GAGCAAGCGC AGGAACAACA G [SEQ ID NO:75]

PMON13044

40 ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
45 CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
TTTTCTCTA CCAGGGGCTC CTGCAGGCCC TGGAAGGGAT ATCCCCCGAG
50 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC
CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
55 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATTT
60

173

5 CCCCCGGGCC TCCTGTCAAT GCTGGCGGCG GCTCTGGTGG TGGTTCTGST
GGCGGCTCTG AGGSGTGGGG CTCTGAGGGT GGCGGTCTG AGGGTGGCGG
CTCTGAGGGT GGCGGTTCGG GTGGCGGCTC CGGTTCGGGT GATTTTGATT
ATGAAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC
10 TTAAAGAGAC CACCTGCACC TTTGCTGGAC CCGAACAACC TCAATGACGA
AGACGTCTCT ATCCTGATGG AACGAAACCT TCGACTTCCA AACCTGGAGA
GCTTCGTAAG GGCTGTCAAG AACTTAGAAA ATGCATCAGG TATTGAGGCA
15 ATTCTTCGTA ATCTCCAACC ATGTCTGCCC TCTGCCACGG CCGCACCCCTC
TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA
AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG
20

[SEQ ID NO:76]

PMON13045

25 ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
30 AGGAGAAGCT GTGTGCCACC TACAAGCTG GCCACCCCGA GGAGCTGGTG
CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
35 TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGGAAGGGAT ATCCCCGAG
TTGGGTCCCA CCTTGGACAC ACTGC G GACGTCGCCG ACTTTGCCAC
40 CACCATCTGG CAGCAGATGG AAGAA G AATGGCCCCCT GCCCTGCAGC
CCACCCAGGS TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
GGAGGGGTCC TGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
45 CCGCGTTCTA CGCCACCTTG CGCACCCTA CGTAATCGAG GGAAGGATTT
CCCCGGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG
TCTAAAGAAT CTCATAAATC TCCAAACATG GCTAACTGCT CTATAATGAT
50 CGATGAAATT ATACATCACT TAAAGAGACC ACCTGCACCT TTGCTGGACC
CGAACAACCT CAATGACGAA GACGTCTCTA TCCTGATGGA ACGAAACCTT
55 GCACTTCCAA ACCTGGAGAG CTTCGTAAGG GCTGTCAAGA ACTTAGAAAA
TGCATCAGGT ATTGAGGCAA TTCTTCGTAA TCTCCAACCA TGTCTGCCCT
60 CTGCCACGGC CGCACCCCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC

174

TGGCAAGAAT TCCGGGAAAA ACTGACGTTT TATCTGGTTA CCCTTGAGCA
AGCGCAGGAA CAACAG [SEQ ID NO:77]

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PMON13151

ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
10 CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
15 CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
TTTTCTCTA CCAGGGGCTC CTGCAGGCCC TGGAAGGGAT ATCCCCCGAG
20 TTGGGTCCCA COTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC
CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
25 GGAGGGGTCC TGTTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
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30 CCCCGGGTGG TGTTCTGGC GCGGCTCCA ACATGGCTAA CTGCTCTATA
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35 ACCTTCGACT TCCAAACCTG GAGAGCTTCG TAAGGGCTGT CAAGAACTTA
GAAAATGCAT CAGGTATTGA GGCAATTCTT CGTAATCTCC AACCATGTCT
40 GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC ATCAAGGCAG
GTGACTGGCA AGAATTCCGG GAAAACTGA CGTCTATCT GGTACCCTT
GAGCAAGCGC AGGAACAACA G [SEQ ID NO:78]

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PMON13152

ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
50 CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
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55 CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
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60

175

5 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
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10 CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
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15 CCGCGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG
TCTAAAGAAT CTCATAAATC TCCAAACATG GCTAACTGCT CTATAATGAT
CGATGAAATT ATACATCACT TAAAGAGACC ACCTGCACCT TTGCTGGACC
CGAACAACCT CAATGACGAA GACGTCTCTA TCCTGATGGA ACGAAACCTT
20 CGACTTCCAA ACCTGGAGAG CTTCGTAAGG GCTGTCAAGA ACTTAGAAAA
TGCATCAGGT ATTGAGGCAA TTCTTCGTAA TCTCCAACCA TGTCTGCCCT
CTGCCACGGC CGCACCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC
25 TGGCAAGAAT TCCGGGAAAA ACTGACGTTT TATCTGGTTA CCCTTGAGCA
AGCGCAGGAA CAACAG [SEQ ID NO:79]

30 PMON13149

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35 CAAGTCTTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
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CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
40 CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
TTTTCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG
45 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC
CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
50 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
CGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC GGTGGAGGCT
CCCCGGGTGG TGGTTCTGGC GGCGGCTCCA ACATGGCTAA CTGCTCTATA
55 ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTG CACCTTGTCT
GGACCCGAAC AACCTCAATG ACGAAGACGT CTCTATCCTG ATGGAACGAA
60 ACCTTCGACT TCCAAACCTG GAGAGCTTCG TAAGGGCTGT CAAGAACTTA

1. 2. 3. 4. 5. 6. 7. 8. 9. 10. 11. 12. 13. 14. 15. 16. 17. 18. 19. 20. 21. 22. 23. 24. 25. 26. 27. 28. 29. 30. 31. 32. 33. 34. 35. 36. 37. 38. 39. 40. 41. 42. 43. 44. 45. 46. 47. 48. 49. 50. 51. 52. 53. 54. 55. 56. 57. 58. 59. 60. 61. 62. 63. 64. 65. 66. 67. 68. 69. 70. 71. 72. 73. 74. 75. 76. 77. 78. 79. 80. 81. 82. 83. 84. 85. 86. 87. 88. 89. 90. 91. 92. 93. 94. 95. 96. 97. 98. 99. 100. 101. 102. 103. 104. 105. 106. 107. 108. 109. 110. 111. 112. 113. 114. 115. 116. 117. 118. 119. 120. 121. 122. 123. 124. 125. 126. 127. 128. 129. 130. 131. 132. 133. 134. 135. 136. 137. 138. 139. 140. 141. 142. 143. 144. 145. 146. 147. 148. 149. 150. 151. 152. 153. 154. 155. 156. 157. 158. 159. 160. 161. 162. 163. 164. 165. 166. 167. 168. 169. 170. 171. 172. 173. 174. 175. 176. 177. 178. 179. 180. 181. 182. 183. 184. 185. 186. 187. 188. 189. 190. 191. 192. 193. 194. 195. 196. 197. 198. 199. 200. 201. 202. 203. 204. 205. 206. 207. 208. 209. 210. 211. 212. 213. 214. 215. 216. 217. 218. 219. 220. 221. 222. 223. 224. 225. 226. 227. 228. 229. 230. 231. 232. 233. 234. 235. 236. 237. 238. 239. 240. 241. 242. 243. 244. 245. 246. 247. 248. 249. 250. 251. 252. 253. 254. 255. 256. 257. 258. 259. 260. 261. 262. 263. 264. 265. 266. 267. 268. 269. 270. 271. 272. 273. 274. 275. 276. 277. 278. 279. 280. 281. 282. 283. 284. 285. 286. 287. 288. 289. 290. 291. 292. 293. 294. 295. 296. 297. 298. 299. 300. 301. 302. 303. 304. 305. 306. 307. 308. 309. 310. 311. 312. 313. 314. 315. 316. 317. 318. 319. 320. 321. 322. 323. 324. 325. 326. 327. 328. 329. 330. 331. 332. 333. 334. 335. 336. 337. 338. 339. 340. 341. 342. 343. 344. 345. 346. 347. 348. 349. 350. 351. 352. 353. 354. 355. 356. 357. 358. 359. 360. 361. 362. 363. 364. 365. 366. 367. 368. 369. 370. 371. 372. 373. 374. 375. 376. 377. 378. 379. 380. 381. 382. 383. 384. 385. 386. 387. 388. 389. 390. 391. 392. 393. 394. 395. 396. 397. 398. 399. 400. 401. 402. 403. 404. 405. 406. 407. 408. 409. 410. 411. 412. 413. 414. 415. 416. 417. 418. 419. 420. 421. 422. 423. 424. 425. 426. 427. 428. 429. 430. 431. 432. 433. 434. 435. 436. 437. 438. 439. 440. 441. 442. 443. 444. 445. 446. 447. 448. 449. 450. 451. 452. 453. 454. 455. 456. 457. 458. 459. 460. 461. 462. 463. 464. 465. 466. 467. 468. 469. 470. 471. 472. 473. 474. 475. 476. 477. 478. 479. 480. 481. 482. 483. 484. 485. 486. 487. 488. 489. 490. 491. 492. 493. 494. 495. 496. 497. 498. 499. 500. 501. 502. 503. 504. 505. 506. 507. 508. 509. 510. 511. 512. 513. 514. 515. 516. 517. 518. 519. 520. 521. 522. 523. 524. 525. 526. 527. 528. 529. 530. 531. 532. 533. 534. 535. 536. 537. 538. 539. 540. 541. 542. 543. 544. 545. 546. 547. 548. 549. 550. 551. 552. 553. 554. 555. 556. 557. 558. 559. 560. 561. 562. 563. 564. 565. 566. 567. 568. 569. 570. 571. 572. 573. 574. 575. 576. 577. 578. 579. 580. 581. 582. 583. 584. 585. 586. 587. 588. 589. 590. 591. 592. 593. 594. 595. 596. 597. 598. 599. 600. 601. 602. 603. 604. 605. 606. 607. 608. 609. 610. 611. 612. 613. 614. 615. 616. 617. 618. 619. 620. 621. 622. 623. 624. 625. 626. 627. 628. 629. 630. 631. 632. 633. 634. 635. 636. 637. 638. 639. 640. 641. 642. 643. 644. 645. 646. 647. 648. 649. 650. 651. 652. 653. 654. 655. 656. 657. 658. 659. 660. 661. 662. 663. 664. 665. 666. 667. 668. 669. 670. 671. 672. 673. 674. 675. 676. 677. 678. 679. 680. 681. 682. 683. 684. 685. 686. 687. 688. 689. 690. 691. 692. 693. 694. 695. 696. 697. 698. 699. 700. 701. 702. 703. 704. 705. 706. 707. 708. 709. 710. 711. 712. 713. 714. 715. 716. 717. 718. 719. 720. 721. 722. 723. 724. 725. 726. 727. 728. 729. 730. 731. 732. 733. 734. 735. 736. 737. 738. 739. 740. 741. 742. 743. 744. 745. 746. 747. 748. 749. 750. 751. 752. 753. 754. 755. 756. 757. 758. 759. 760. 761. 762. 763. 764. 765. 766. 767. 768. 769. 770. 771. 772. 773. 774. 775. 776. 777. 778. 779. 780. 781. 782. 783. 784. 785. 786. 787. 788. 789. 790. 791. 792. 793. 794. 795. 796. 797. 798. 799. 800. 801. 802. 803. 804. 805. 806. 807. 808. 809. 810. 811. 812. 813. 814. 815. 816. 817. 818. 819. 820. 821. 822. 823. 824. 825. 826. 827. 828. 829. 830. 831. 832. 833. 834. 835. 836. 837. 838. 839. 840. 84

177

5 AGGGCTGTCA AGAACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
10 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTAACTGC
15 TCTATAATGA TCGATGAAAT TATACATCAC TTAAAGAGAC CACCTGCACC
TTTGCTGGAC CCGAACAACC TCAATGACGA AGACGTCTCT ATCCTGATGG
AACGAAACCT TCGACTTCCA AACCTGGAGA GCTTCGTAAG GGCTGTCAAG
20 AACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC
ATGTCTGCCC TCTGCCACGG CCGCACCCCTC TCGACATCCA ATCATCATCA
AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA AACTGACGTT CTATCTGGTT
25 ACCCTTGAGC AAGCGCAGGA ACAACAG [SEQ ID NO:82]

30 PMON13053
ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
35 ACCACCTGCA CCTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT
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40 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
45 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
GGGAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTACACCA
50 TTGGGCCCCTG CCAGCTCCCT GCCCCAGAGC TTCCTGCTCA AGTCTTTAGA
GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG GAGAAGCTGT
GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC
55 TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT
GCAGCTGGCA GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC
60 AGGGGCTCCT GCAGGCCCTG GAAGGATAT CCCCCGAGTT GGGTCCCACC

179

AGGGCTGTCA AGAACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
5 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
10 GGAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
CACCATTGGG CCCTGCCAGC TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT
TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA
15 GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG
GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG
GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT
20 CTACCAGGGG CTCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC
CCACCTTGA CACACTGCAG CTGGACGTCG CCGACTTTGC CACCACCATC
TGGCAGCAGA TGGAAGAACT GGAATGGCC CCTGCCCTGC AGCCCACCCA
GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG GCAGGAGGGG
30 TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT
CTACGCCACC TTGCGCAGCC C [SEQ ID NO:85]

35 PMON13050

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
40 ACCACCTGCA CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT
CTATCCTGAT GGAACGAAAC CTTGCACTTC CAAACCTGGA GAGCTTCGTA
AGGGCTGTCA AGAACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
45 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
50 GGAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
ACTGCTCTAT AATGATCGAT GAAATTATAC ATCACTTAAA GAGACCACCT
55 GCACCTTTGC TGGACCCGAA CAACCTCAAT GACGAAGACG TCTCTATCCT
GATGGAACGA AACCTTCGAC TTCCAAACCT GGAGAGCTTC GTAAGGGCTG
TCAAGAACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC
60

The first part of the document discusses the importance of maintaining accurate records of all transactions. It emphasizes that every entry, no matter how small, should be recorded to ensure the integrity of the financial data. This includes not only sales and purchases but also expenses and income. The second part of the document provides a detailed breakdown of the company's revenue for the quarter. It shows that sales have increased by 15% compared to the previous quarter, which is a positive trend. However, it also notes that expenses have increased by 10%, which has slightly reduced the overall profit margin. The third part of the document discusses the company's financial position at the end of the quarter. It shows that the company is in a strong financial position, with a healthy cash flow and a low level of debt. The fourth part of the document provides a summary of the company's performance for the quarter and offers some recommendations for the future. It suggests that the company should continue to focus on increasing sales and controlling expenses to improve its profit margin. It also recommends that the company should consider investing in new equipment and technology to improve its operational efficiency.

10/10/2023
10/11/2023
10/12/2023
10/13/2023
10/14/2023

181

CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
5 CGGTGGAGGC TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
ACTGCTCTAT AATGATCGAT GAAATTATAC ATCACTTAAA GAGACCACCT
GCACCTTTGC TGGACCCGAA CAACCTCAAT GACGAAGACG TCTCTATCCT
10 GATGGAACGA AACCTTCGAC TTCCAAACCT GGAGAGCTTC GTAAGGGCTG
TCAAGAACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC
CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT
15 CATCAAGGCA GGTGACTGGC AAGAATTCCG GGAAAACTG ACGTTCTATC
TGGTTACCCT TGAGCAAGCG CAGGAACAAC AG [SEQ ID NO:88]
20

PMON13146

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25 ACCACCTGCA CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT
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30 AGGGCTGTCA AGAACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
35 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
CGGTGGAGGC TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
40 CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTACACCA
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GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG GAGAAGCTGT
45 GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC
TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT
50 GCAGCTGGCA GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC
AGGGGCTCCT GCAGGCCCTG GAAGGGATAT CCCCCGAGTT GGGTCCCACC
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55 GCAGATGGAA GAACTGGGAA TGGCCCCTGC CCTGCAGCCC ACCCAGGGTG
CCATGCCGGC CTTGCTCTCT GCTTCCAGC GCCGGGCAGG AGGGGTCTCTG
60 GTTGCTAGCC ATCTGCAGAG CTCCTGGAG GTGTCTGACC GCGTTCTACG

183

CATTCTGCGC AGCTTTAAGG AGTTCCTGCA GTCCAGCCTG AGGGCTCTTC
GGCAAATGTA G [SEQ ID NO:175]

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pMON13012

10

ATGGCACCGG CTCGTTCCCC GTCCCCGTCT ACCCAGCCGT GGGAACACGT
GAATGCCATC CAGGAGGCCC GCGCTCTCCT GAACCTGAGT AGAGACACTG
15 CTGCTGAGAT GAATGAAACA GTAGAAGTGA TATCAGAAAT GTTTGACCTC
CAGGAGCCGA CTGCTCTACA GACCCGCTG GAGCTGTACA AGCAGGGCCT
GCGGGGCAGC CTCACCAAGC TCAAGGGCCC CTTGACCATG ATGGCCAGCC
20 ACTACAAGCA GCACTGCCCT CCAACCCCGG AAACCTCCTG TGCAACCCAG
ATTATCACCT TTGAAAGTTT CAAAGAGAAC CTGAAGGACT TCCTGCTTGT
25 CATCCCCTTT GACTGCTGGG AGCCAGTCCA GGAGTGATAA GGATCCGAAT
TC [SEQ ID NO:176]

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pMON13499

35

ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
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AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
CTGCTCGGAC ACTCTCTGGG CATCCCCTGG GCTCCCCTGA GCTCCTGCCC
40 CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGGAAGGGAT ATCCCCGAG
TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
45 CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCCCT GCCCTGCAGC
CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
50 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
CCGCGTTCTA CGCCACCTTG CGCAGCCCTG ATAAGGATCC GAATTC
[SEQ ID NO:177]

55

pMON13498/pMON13010

60

ATGGCTACAC CATTAGGACC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT

185

AGCAGTGACC CTTCTGCTGG AGGGAGTGAT GGCAGCACGG GGACAACTGG
GACCCACTTG CCTCTCATCC CTCCTGGGGC AGCTTTCTGG ACAGGTCCGT
5 CTCCTCCTTG GGGCCCTGCA GAGCCTCCTT GGAACCCAGC TTCCTCCACA
GGGCAGGACC ACAGCTCACA AGGATCCCAA TGCCATCTTC CTGAGGTTCC
10 AACACCTGCT CCGAGGAAAG GTGCGTTTCC TGATGCTTGT AGGAGSGTCC
ACCCTCTGCG TCAGG [SEQ ID NO:180]

pMON26463

15 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
20 ATATCCTGAT GGAACGAAAC CTTGGAAGTC CAAACCTGCT CGCATTTCGT
AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
25 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCGGGGA AAAACTGACG
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
30 GGAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCGT
CTCCGGCGCC GCCTGCTTGT GACCTCCGAG TCCTCAGTAA ACTGCTTCGT
GACTCCCATG TCCTTCACAG CAGACTGAGC CAGTGCCAG AGGTTACCCC
35 TTTGCCTACA CCTGTCCTGC TGCCTCTGT GGACTTTAGC TTGGGAGAAT
GGAAAACCCA GATGGAGGAG ACCAAGGCAC AGGACATTCT GGGAGCAGTG
40 ACCCTTCTGC TGGAGGGAGT GATGGCAGCA CGGGGACAAC TGGGACCCAC
TTGCCTCTCA TCCCTCCTGG GGCAGCTTTC TGGACAGGTC CGTCTCCTCC
TTGGGGCCCT GCAGAGCCTC CTTGGAACCC AGCTTCCTCC ACAGGGCAGG
45 ACCACAGCTC ACAAGGATCC CAATGCCATC TTCCTGAGCT TCCAACACCT
GCTCCGAGGA AAGGTGCGTT TCCTGATGCT TGTAGGAGGG TCCACCCTCT
50 GCGTCAGG [SEQ ID NO:183]

pMON26473

55 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
60 ATATCCTGAT GGAACGAAAC CTTGGAAGTC CAAACCTGCT CGCATTTCGT

187

5 GCTCGCATTC GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG
AGGCAATTCT TCGTAATCTC CAACCATGTC TGCCCTCTGC CACGGCCGCA
CCCTCTCGAC ATCCAATCAT CATCAAGGCA GGTGACTGGC AAGAATTCCG
GGAAAACTG ACGTTCTATC TGCTTACCCT TGAGCAAGCG CAGGAACAAC
10 AG [SEQ ID NO:185]

PMON26464
15 ATGGCGTCTC CGGCGCCGCC TGCTTGTGAC CTCCGAGTCC TCAGTAAACT
GCTTCGTGAC TCCCATGTCC TTCACAGCAG ACTGAGCCAG TGCCCAGAGG
20 TTCACCTTT GCCTACACCT GTCCTGCTGC CTGCTGTGGA CTTTAGCTTG
GGAGAATGGA AAACCCAGAT GGAGGAGACC AAGGCACAGG ACATTCTGGG
AGCAGTGACC CTTCTGCTGG AGGGAGTGAT GGCAGCACGG GGACAACTGG
25 GACCCACTTG CCTCTCATCC CTCCTGGGGC AGCTTTCTGG ACAGGTCCGT
CTCCTCCTTG GGGCCCTGCA GAGCCTCCTT GGAACCCAGC TTCCTCCACA
GGGCAGGACC ACAGCTCACA AGGATCCCAA TGCCATCTTC CTGAGCTTCC
30 AACACCTGCT CCGAGGAAAG GTGCGTTTCC TGATGCTTGT AGGAGGGTCC
ACCCTCTGCG TCAGGGAATT CCATGCATAC GTAGAGGGCG GTGGAGGCTC
35 CCCGGGTGGT GGTTCCTGGCG GCGGCTCCAA CATGGCTAAC TGCTCTATAA
TGATCGATGA AATTATACAT CACTTAAAGA GACCACCTA CCCTTTGCTG
GACCCGAACA ACCTCAATTC TGAAGACATG GATATCCTGA TGAACGAAA
40 CCTTCGAACT CCAAACCTGC TCGCATTCGT AAGGGCTGTC AAGCACTTAG
AAAATGCATC AGGTATTGAG GCAATTCTTC GTAATCTCCA ACCATGTCTG
45 CCCTCTGCCA CGGCCGCACC CTCTCGACAT CCAATCATCA TCAAGGCAGG
TGACTGGCAA GAATCCGGG AAAAAGTAC GTTCTATCTG GTTACCCTTG
50 AGCAAGCGCA GGAACAACAG [SEQ ID NO:186]

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A simple method using two oligonucleotide primers and a single-
stranded DNA template. DNA, 3: 479 (1984).
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-201-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /note= "Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /note= "Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /note= "Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /note= "Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, Asn, Thr, Ser, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 22
- (D) OTHER INFORMATION: /note= "Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, Gln, Leu, Val, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 23
- (D) OTHER INFORMATION: /note= "Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys, Phe, Ser, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 24
- (D) OTHER INFORMATION: /note= "Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 25
- (D) OTHER INFORMATION: /note= "Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 26
- (D) OTHER INFORMATION: /note= "Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 27
- (D) OTHER INFORMATION: /note= "Xaa at position 27 is Leu,

-203-

Ser, Pro, Trp, or Ile"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 38

(D) OTHER INFORMATION: /note= "Xaa at position 38 is Asn,
or Ala"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 40

(D) OTHER INFORMATION: /note= "Xaa at position 40 is Leu,
Trp, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 41

(D) OTHER INFORMATION: /note= "Xaa at position 41 is Asn,
Cys, Arg, Leu, His, Met, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 42

(D) OTHER INFORMATION: /note= "Xaa at position 42 is Gly,
Asp, Ser, Cys, Asn, Lys, Thr, Leu, Val, Glu, Phe, Tyr,
Ile, Met, or Ala"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 43

(D) OTHER INFORMATION: /note= "Xaa at position 43 is Glu,
Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg, Thr, Gly,
or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 44

(D) OTHER INFORMATION: /note= "Xaa at position 44 is Asp,
Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala,
or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 45

(D) OTHER INFORMATION: /note= "Xaa at position 45 is Gln,
Pro, Phe, Val, Met, Leu, Thr, Lys, Trp, Asp, Asn, Arg,
Ser, Ala, Ile, Glu, or His"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 46

(D) OTHER INFORMATION: /note= "Xaa at position 46 is Asp,
Phe, Ser, Thr, Cys, Glu, Asn, Gln, Lys, His, Ala, Tyr,
Ile, Val, or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 47

(D) OTHER INFORMATION: /note= "Xaa at position 47 is Ile,
Gly, Val, Ser, Arg, Pro, or His"

-205-

(D) OTHER INFORMATION: /note= "Xaa at position 57 is Asn or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 58

(D) OTHER INFORMATION: /note= "Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 59

(D) OTHER INFORMATION: /note= "Xaa at position 59 is Glu, Tyr, His, Leu, Pro, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 60

(D) OTHER INFORMATION: /note= "Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 61

(D) OTHER INFORMATION: /note= "Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 62

(D) OTHER INFORMATION: /note= "Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 63

(D) OTHER INFORMATION: /note= "Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 64

(D) OTHER INFORMATION: /note= "Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 65

(D) OTHER INFORMATION: /note= "Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 66

(D) OTHER INFORMATION: /note= "Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 67

(D) OTHER INFORMATION: /note= "Xaa at position 67 is Ser,

-207-

(D) OTHER INFORMATION: /note= "Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 78

(D) OTHER INFORMATION: /note= "Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 79

(D) OTHER INFORMATION: /note= "Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or Asp"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 80

(D) OTHER INFORMATION: /note= "Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 81

(D) OTHER INFORMATION: /note= "Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or Lys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 82

(D) OTHER INFORMATION: /note= "Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met, or Val"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 83

(D) OTHER INFORMATION: /note= "Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 84

(D) OTHER INFORMATION: /note= "Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 85

(D) OTHER INFORMATION: /note= "Xaa at position 85 is Leu, Asn, Val, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 86

(D) OTHER INFORMATION: /note= "Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 87

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-209-

(D) OTHER INFORMATION: /note= "Xaa at position 97 is Ile, Val, Lys, Ala, or Asn"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 98

(D) OTHER INFORMATION: /note= "Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 99

(D) OTHER INFORMATION: /note= "Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln, Gly, Ser, Phe, or His"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 100

(D) OTHER INFORMATION: /note= "Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 101

(D) OTHER INFORMATION: /note= "Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val, Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 102

(D) OTHER INFORMATION: /note= "Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 103

(D) OTHER INFORMATION: /note= "Xaa at position 103 is Asp, or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 104

(D) OTHER INFORMATION: /note= "Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, Gln, Lys, Ala, Phe, or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 105

(D) OTHER INFORMATION: /note= "Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, Leu, Lys, Ile, Asp, or His"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 106

(D) OTHER INFORMATION: /note= "Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro"

-211-

(D) OTHER INFORMATION: /note= "Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 118

(D) OTHER INFORMATION: /note= "Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 119

(D) OTHER INFORMATION: /note= "Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 120

(D) OTHER INFORMATION: /note= "Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 121

(D) OTHER INFORMATION: /note= "Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 122

(D) OTHER INFORMATION: /note= "Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 123

(D) OTHER INFORMATION: /note= "Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Pro | Met | Thr | Gln | Thr | Thr | Ser | Leu | Lys | Thr | Ser | Trp | Val | Asn | Cys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Asn | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | | 35 | | | | 40 | | | | | | 45 | | |
| Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | | 50 | | | | 55 | | | | | 60 | | | |
| Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | | | | 85 | | | | | 90 | | | | | 95 |

-213-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 25
- (D) OTHER INFORMATION: /note= "Xaa at position 25 is Thr, His, Gln, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 26
- (D) OTHER INFORMATION: /note= "Xaa at position 26 is His or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 29
- (D) OTHER INFORMATION: /note= "Xaa at position 29 is Gln, Asn, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 30
- (D) OTHER INFORMATION: /note= "Xaa at position 30 is Pro, Gly, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 31
- (D) OTHER INFORMATION: /note= "Xaa at position 31 is Pro, Asp, Gly, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 32
- (D) OTHER INFORMATION: /note= "Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 33
- (D) OTHER INFORMATION: /note= "Xaa at position 33 is Pro or Glu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 34
- (D) OTHER INFORMATION: /note= "Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 35
- (D) OTHER INFORMATION: /note= "Xaa at position 35 is Leu, Ala, Asn, Pro, Gln, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 37
- (D) OTHER INFORMATION: /note= "Xaa at position 37 is Phe, Ser, Pro, or Trp"

(ix) FEATURE:

-215-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 60
- (D) OTHER INFORMATION: /note= "Xaa at position 60 is Ala or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 62
- (D) OTHER INFORMATION: /note= "Xaa at position 62 is Asn, Pro, Thr, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 63
- (D) OTHER INFORMATION: /note= "Xaa at position 63 is Arg or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 64
- (D) OTHER INFORMATION: /note= "Xaa at position 64 is Ala or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 65
- (D) OTHER INFORMATION: /note= "Xaa at position 65 is Val or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 66
- (D) OTHER INFORMATION: /note= "Xaa at position 66 is Lys or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 67
- (D) OTHER INFORMATION: /note= "Xaa at position 67 is Ser Phe or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 68
- (D) OTHER INFORMATION: /note= "Xaa at position 68 is Leu, Ile, Phe, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 69
- (D) OTHER INFORMATION: /note= "Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 71
- (D) OTHER INFORMATION: /note= "Xaa at position 71 is Ala, Pro, or Arg"

-217-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 88
- (D) OTHER INFORMATION: /note= "Xaa at position 88 is Ala or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 91
- (D) OTHER INFORMATION: /note= "Xaa at position 91 is Ala or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 93
- (D) OTHER INFORMATION: /note= "Xaa at position 93 is Thr, Asp, Ser, Pro, Ala, Leu, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 95
- (D) OTHER INFORMATION: /note= "Xaa at position 95 is His, Pro, Arg, Val, Leu, Gly, Asn, Phe, Ser, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 96
- (D) OTHER INFORMATION: /note= "Xaa at position 96 is Pro or Tyr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 97
- (D) OTHER INFORMATION: /note= "Xaa at position 97 is Ile or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is His, Ile, Asn, Leu, Ala, Thr, Arg, Gln, Lys, Met, Ser, Tyr, Val, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 99
- (D) OTHER INFORMATION: /note= "Xaa at position 99 is Ile, Leu, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 100
- (D) OTHER INFORMATION: /note= "Xaa at position 100 is Lys, Arg, Ile, Gln, Pro, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 101
- (D) OTHER INFORMATION: /note= "Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Asn, Ile, Leu, or Tyr"

-219-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 120
- (D) OTHER INFORMATION: /note= "Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 121
- (D) OTHER INFORMATION: /note= "Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Asp, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 122
- (D) OTHER INFORMATION: /note= "Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 123
- (D) OTHER INFORMATION: /note= "Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Pro | Met | Thr | Gln | Thr | Thr | Ser | Leu | Lys | Thr | Ser | Trp | Val | Asn | Cys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Xaa | Xaa | Xaa | Ile | Xaa | Glu | Xaa | Xaa | Xaa | Xaa | Leu | Lys | Xaa | Xaa | Xaa | Xaa |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Xaa | Xaa | Xaa | Asp | Xaa | Xaa | Asn | Leu | Asn | Xaa | Glu | Xaa | Xaa | Xaa | Ile | Leu |
| | | | 35 | | | | 40 | | | | | 45 | | | |
| Met | Xaa | Xaa | Asn | Leu | Xaa | Xaa | Xaa | Asn | Leu | Glu | Xaa | Phe | Xaa | Xaa | Xaa |
| | | | 50 | | | | 55 | | | | 60 | | | | |
| Xaa | Xaa | Xaa | Xaa | Xaa | Asn | Xaa | Xaa | Xaa | Ile | Glu | Xaa | Xaa | Leu | Xaa | Xaa |
| 65 | | | | | 70 | | | | | 75 | | | | 80 | |
| Leu | Xaa | Xaa | Cys | Xaa | Pro | Xaa | Xaa | Thr | Ala | Xaa | Pro | Xaa | Arg | Xaa | Xaa |
| | | | 85 | | | | | | 90 | | | | | 95 | |
| Xaa | Xaa | Xaa | Xaa | Xaa | Gly | Asp | Xaa | Xaa | Xaa | Phe | Xaa | Xaa | Lys | Leu | Xaa |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Phe | Xaa | Xaa | Xaa | Xaa | Leu | Glu | Xaa | Xaa | Xaa | Xaa | Gln | Gln | Thr | Thr | Leu |
| | | | 115 | | | | | 120 | | | | | 125 | | |
| Ser | Leu | Ala | Ile | Phe | | | | | | | | | | | |
| | | | 130 | | | | | | | | | | | | |

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 133 amino acids
- (B) TYPE: amino acid

-221-

- (B) LOCATION: 34
- (D) OTHER INFORMATION: /note= "Xaa at position 34 is Leu, Val, Ser, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 35
- (D) OTHER INFORMATION: /note= "Xaa at position 35 is Leu, Ala, Asn, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 38
- (D) OTHER INFORMATION: /note= "Xaa at position 38 is Asn or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 42
- (D) OTHER INFORMATION: /note= "Xaa at position 42 is Gly, Asp, Ser, Ala, Asn, Ile, Leu, Met, Tyr, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 45
- (D) OTHER INFORMATION: /note= "Xaa at position 45 is Gln, Val, Met, Leu, Ala, Asn, Glu, or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 46
- (D) OTHER INFORMATION: /note= "Xaa at position 46 is Asp, Phe, Ser, Gln, Glu, His, Val, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 50
- (D) OTHER INFORMATION: /note= "Xaa at position 50 is Glu, Asn, Ser, or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 51
- (D) OTHER INFORMATION: /note= "Xaa at position 51 is Asn, Arg, Pro, Thr, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 55
- (D) OTHER INFORMATION: /note= "Xaa at position 55 is Arg, Leu, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 56
- (D) OTHER INFORMATION: /note= "Xaa at position 56 is Pro, Gly, Ser, Ala, Asn, Val, Leu, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 62

-223-

Gln, Trp, Arg, Asp, Asn, Glu, His, Met, Phe, Ser,
Thr, Tyr, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 87
- (D) OTHER INFORMATION: /note= "Xaa at position 87 is Leu or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 88
- (D) OTHER INFORMATION: /note= "Xaa at position 88 is Ala or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 91
- (D) OTHER INFORMATION: /note= "Xaa at position 91 is Ala or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 93
- (D) OTHER INFORMATION: /note= "Xaa at position 93 is Thr, Asp, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 95
- (D) OTHER INFORMATION: /note= "Xaa at position 95 is His, Pro, Arg, Val, Gly, Asn, Ser, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is His, Ile, Asn, Ala, Thr, Gln, Glu, Lys, Met, Ser, Tyr, Val, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 99
- (D) OTHER INFORMATION: /note= "Xaa at position 99 is Ile or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 100
- (D) OTHER INFORMATION: /note= "Xaa at position 100 is Lys or Arg"

(ix) FEATURE;

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 101
- (D) OTHER INFORMATION: /note= "Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Asn, Ile, Leu, or Tyr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 105

-225-

Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa Xaa Pro Xaa
 20 25 30
 Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa Ile Leu
 35 40 45
 Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala Phe Xaa Arg Xaa
 50 55 60
 Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu Xaa Xaa Leu Xaa Xaa
 65 70 75 80
 Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala Xaa Pro Xaa Arg Xaa Pro
 85 90 95
 Ile Xaa Xaa Xaa Xaa Gly Asp Trp Xaa Glu Phe Xaa Xaa Lys Leu Xaa
 100 105 110
 Phe Tyr Leu Xaa Xaa Leu Glu Xaa Xaa Xaa Xaa Gln Gln Thr Thr Leu
 115 120 125
 Ser Leu Ala Ile Phe
 130

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /note= "Met- or Met-Ala- may or may not precede the amino acid in position 1"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /note= "Xaa at position 3 is Ser, Lys, Gly, Asp, Met, Gln, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /note= "Xaa at position 4 is Asn, His, Leu, Ile, Phe, Arg, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /note= "Xaa at position 5 is Met, Phe, Ile, Arg, Gly, Ala, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

-227-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /note= "Xaa at position 16 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 17
- (D) OTHER INFORMATION: /note= "Xaa at position 17 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /note= "Xaa at position 18 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or Glu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /note= "Xaa at position 19 is Pro, Leu, Gln, Ala, Thr, or Glu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /note= "Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr, Arg, Ala, Phe, Ile, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /note= "Xaa at position 21 is Leu, Ala, Gly, Asn, Pro, Gln, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 22
- (D) OTHER INFORMATION: /note= "Xaa at position 22 is Asp, Leu, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 23
- (D) OTHER INFORMATION: /note= "Xaa at position 23 is Phe, Ser, Pro, Trp, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 24
- (D) OTHER INFORMATION: /note= "Xaa at position 24 is Asn or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 26
- (D) OTHER INFORMATION: /note= "Xaa at position 26 is Leu, Trp, or Arg"

-229-

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 36
- (D) OTHER INFORMATION: /note= "Xaa at position 36 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, Ala, Ile, Val, His, Phe, Met, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 37
- (D) OTHER INFORMATION: /note= "Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 38
- (D) OTHER INFORMATION: /note= "Xaa at position 38 is Asn, His, Arg, Leu, Gly, Ser, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 39
- (D) OTHER INFORMATION: /note= "Xaa at position 39 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 40
- (D) OTHER INFORMATION: /note= "Xaa at position 40 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 41
- (D) OTHER INFORMATION: /note= "Xaa at position 41 is Arg, Thr, Val, Ser, Leu, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 42
- (D) OTHER INFORMATION: /note= "Xaa at position 42 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, Phe, Leu, Val, or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 43
- (D) OTHER INFORMATION: /note= "Xaa at position 43 is Asn or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 44
- (D) OTHER INFORMATION: /note= "Xaa at position 44 is Leu, Ser, Asp, Arg, Gln, Val, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 45
- (D) OTHER INFORMATION: /note= "Xaa at position 45 is Glu, Tyr, His, Leu, Pro, or Arg"

-231-

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 56
- (D) OTHER INFORMATION: /note= "Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 57
- (D) OTHER INFORMATION: /note= "Xaa at position 57 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, Trp, or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 58
- (D) OTHER INFORMATION: /note= "Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 59
- (D) OTHER INFORMATION: /note= "Xaa at position 59 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 60
- (D) OTHER INFORMATION: /note= "Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 61
- (D) OTHER INFORMATION: /note= "Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 62
- (D) OTHER INFORMATION: /note= "Xaa at position 62 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 63
- (D) OTHER INFORMATION: /note= "Xaa at position 63 is Ile, Ser, Arg, Thr, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 64
- (D) OTHER INFORMATION: /note= "Xaa at position 64 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 65
- (D) OTHER INFORMATION: /note= "Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile, or Asp"

(ix) FEATURE:

-233-

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 76
- (D) OTHER INFORMATION: /note= "Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 77
- (D) OTHER INFORMATION: /note= "Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 78
- (D) OTHER INFORMATION: /note= "Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, Ile, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 79
- (D) OTHER INFORMATION: /note= "Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 80
- (D) OTHER INFORMATION: /note= "Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, His, Ala, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 81
- (D) OTHER INFORMATION: /note= "Xaa at position 81 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 82
- (D) OTHER INFORMATION: /note= "Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 83
- (D) OTHER INFORMATION: /note= "Xaa at position 83 is Ile, Val, Lys, Ala, or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 84
- (D) OTHER INFORMATION: /note= "Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr, Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 85
- (D) OTHER INFORMATION: /note= "Xaa at position 85 is Ile, Leu, Arg, Asp, Val, Pro, Gln, Gly, Ser, Phe, or His"

10/10/10

10/10/10

10/10/10

10/10/10

-235-

Asn, Thr, Leu, Gln, Arg, His, Glu, Ser, Ala,
or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 97
- (D) OTHER INFORMATION: /note= "Xaa at position 97 is Leu,
Ile, Arg, Asp, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is Thr,
Val, Gln, Tyr, Glu, His, Ser, or Phe"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 99
- (D) OTHER INFORMATION: /note= "Xaa at position 99 is Phe,
Ser, Cys, His, Gly, Trp, Tyr, Asp, Lys, Leu, Ile,
Val, or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 100
- (D) OTHER INFORMATION: /note= "Xaa at position 100 is Tyr,
Cys, His, Ser, Trp, Arg, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 101
- (D) OTHER INFORMATION: /note= "Xaa at position 101 is Leu,
Asn, Val, Pro, Arg, Ala, His, Thr, Trp, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 102
- (D) OTHER INFORMATION: /note= "Xaa at position 102 is
Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, Arg, Trp,
Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 103
- (D) OTHER INFORMATION: /note= "Xaa at position 103 is Thr,
Ser, Asn, Ile, Trp, Lys, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 104
- (D) OTHER INFORMATION: /note= "Xaa at position 104 is Leu,
Ser, Pro, Ala, Glu, Cys, Asp, or Tyr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 105
- (D) OTHER INFORMATION: /note= "Xaa at position 105 is Glu,
Ser, Lys, Pro, Leu, Thr, Tyr, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

-237-

not precede the amino acid in position 1"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /note= "Xaa at position 3 is Ser, Gly, Asp, Met, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /note= "Xaa at position 4 is Asn, His, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /note= "Xaa at position 5 is Met or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (C) OTHER INFORMATION: /note= "Xaa at position 7 is Asp or Glu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /note= "Xaa at position 9 is Ile, Ala, Leu, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /note= "Xaa at position 10 is Ile, Val, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /note= "Xaa at position 11 is Thr, His, Gln, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /note= "Xaa at position 12 is His or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /note= "Xaa at position 15 is Gln, Asn, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /note= "Xaa at position 16 is Pro, Gly, or Gln"

-239-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 32
- (D) OTHER INFORMATION: /note= "Xaa at position 32 is Asp, Phe, Ser, Thr, Ala, Asn, Gln, Glu, His, Ile, Lys, Tyr, Val, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 36
- (D) OTHER INFORMATION: /note= "Xaa at position 36 is Glu, Ala, Asn, Ser, or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 37
- (D) OTHER INFORMATION: /note= "Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 40
- (D) OTHER INFORMATION: /note= "Xaa at position 40 is Arg or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 41
- (D) OTHER INFORMATION: /note= "Xaa at position 41 is Arg, Thr, Val, Leu, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 42
- (D) OTHER INFORMATION: /note= "Xaa at position 42 is Pro, Gly, Ser, Gln, Ala, Arg, Asn, Glu, Leu, Thr, Val, or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 46
- (D) OTHER INFORMATION: /note= "Xaa at position 46 is Ala or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 48
- (D) OTHER INFORMATION: /note= "Xaa at position 48 is Asn, Pro, Thr, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 49
- (D) OTHER INFORMATION: /note= "Xaa at position 49 is Arg or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 50
- (D) OTHER INFORMATION: /note= "Xaa at position 50 is Ala or Asn"

-241-

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 65
- (D) OTHER INFORMATION: /note= "Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile, Gly, or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 66
- (D) OTHER INFORMATION: /note= "Xaa at position 66 is Asn, Gly, Glu, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 68
- (D) OTHER INFORMATION: /note= "Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Ala, Asn, Glu, His, Ile, Met, Phe, Ser, Thr, Tyr, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 69
- (D) OTHER INFORMATION: /note= "Xaa at position 69 is Pro or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 71
- (D) OTHER INFORMATION: /note= "Xaa at position 71 is Leu or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 73
- (D) OTHER INFORMATION: /note= "Xaa at position 73 is Leu or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 74
- (D) OTHER INFORMATION: /note= "Xaa at position 74 is Ala or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 77
- (D) OTHER INFORMATION: /note= "Xaa at position 77 is Ala or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 79
- (D) OTHER INFORMATION: /note= "Xaa at position 79 is Thr, Asp, Ser, Pro, Ala, Leu, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 81
- (D) OTHER INFORMATION: /note= "Xaa at position 81 is His, Pro, Arg, Val, Leu, Gly, Asn, Phe, Ser, or Thr"

(ix) FEATURE:

-243-

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 95
- (D) OTHER INFORMATION: /note= "Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is Thr, Val, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 100
- (D) OTHER INFORMATION: /note= "Xaa at position 100 is Tyr or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 101
- (D) OTHER INFORMATION: /note= "Xaa at position 101 is Leu or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 102
- (D) OTHER INFORMATION: /note= "Xaa at position 102 is Lys, Thr, Val, Trp, Ser, Ala, His, Met, Phe, Tyr, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 103
- (D) OTHER INFORMATION: /note= "Xaa at position 103 is Thr or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 106
- (D) OTHER INFORMATION: /note= "Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 107
- (D) OTHER INFORMATION: /note= "Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Asp, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 108
- (D) OTHER INFORMATION: /note= "Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 109
- (D) OTHER INFORMATION: /note= "Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

-245-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /note= "Xaa at position 12 is His or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /note= "Xaa at position 15 is Gln or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /note= "Xaa at position 16 is Pro or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /note= "Xaa at position 18 is Leu, Arg, Asn, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /note= "Xaa at position 20 is Leu, Val, Ser, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /note= "Xaa at position 21 is Leu, Ala, Asn, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 24
- (D) OTHER INFORMATION: /note= "Xaa at position 24 is Asn or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 28
- (D) OTHER INFORMATION: /note= "Xaa at position 28 is Gly, Asp, Ser, Ala, Asn, Ile, Leu, Met, Tyr, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 31
- (D) OTHER INFORMATION: /note= "Xaa at position 31 is Gln, Val, Met, Leu, Ala, Asn, Glu, or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 32
- (D) OTHER INFORMATION: /note= "Xaa at position 32 is Asp, Phe, Ser, Ala, Gln, Glu, His, Val, or Thr"

(ix) FEATURE:

-247-

- (B) LOCATION: 62
- (D) OTHER INFORMATION: /note= "Xaa at position 62 is Ser, Val, Asn, Pro, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 63
- (D) OTHER INFORMATION: /note= "Xaa at position 63 is Ile or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 65
- (D) OTHER INFORMATION: /note= "Xaa at position 65 is Lys, Asn, Met, Arg, Ile, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 66
- (D) OTHER INFORMATION: /note= "Xaa at position 66 is Asn, Gly, Glu, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 68
- (D) OTHER INFORMATION: /note= "Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Asn, Glu, His, Met, Phe, Ser, Thr, Tyr, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 73
- (D) OTHER INFORMATION: /note= "Xaa at position 73 is Leu or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 74
- (D) OTHER INFORMATION: /note= "Xaa at position 74 is Ala or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 77
- (D) OTHER INFORMATION: /note= "Xaa at position 77 is Ala or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 79
- (D) OTHER INFORMATION: /note= "Xaa at position 79 is Thr, Asp, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 81
- (D) OTHER INFORMATION: /note= "Xaa at position 81 is His, Pro, Arg, Val, Gly, Asn, Ser, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

-249-

(B) LOCATION: 106

(D) OTHER INFORMATION: /note= "Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 107

(D) OTHER INFORMATION: /note= "Xaa at position 107 is Ala, Ser, Ile, Pro, or Asp"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 108

(D) OTHER INFORMATION: /note= "Xaa at position 108 is Gln, Met, Trp, Phe, Pro, His, Ile, or Tyr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 109

(D) OTHER INFORMATION: /note= "Xaa at position 109 is Ala, Met, Glu, Ser, or Leu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

```

Asn Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa Xaa
1           5           10           15
Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa
20           25           30
Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala Phe Xaa
35           40           45
Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu Xaa Xaa Leu
50           55           60
Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala Xaa Pro Xaa Arg
65           70           75           80
Xaa Pro Ile Xaa Xaa Xaa Xaa Gly Asp Trp Xaa Glu Phe Xaa Xaa Lys
85           90           95
Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu Xaa Xaa Xaa Xaa Gln Gln
100          105          110

```

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 133 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 1

(D) OTHER INFORMATION: /note= "Met- may or may not precede"

-251-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 42
- (D) OTHER INFORMATION: /note= "Xaa at position 42 is Gly, Ala, Ser, Asp, or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 45
- (D) OTHER INFORMATION: /note= "Xaa at position 45 is Gln, Val, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 46
- (D) OTHER INFORMATION: /note= "Xaa at position 46 is Asp or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 49
- (D) OTHER INFORMATION: /note= "Xaa at position 49 is Met, Ile, Leu, or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 50
- (D) OTHER INFORMATION: /note= "Xaa at position 50 is Glu or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 51
- (D) OTHER INFORMATION: /note= "Xaa at position 51 is Asn, Arg, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 55
- (D) OTHER INFORMATION: /note= "Xaa at position 55 is Arg, Leu, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 56
- (D) OTHER INFORMATION: /note= "Xaa at position 56 is Pro or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 59
- (D) OTHER INFORMATION: /note= "Xaa at position 59 is Glu or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 60
- (D) OTHER INFORMATION: /note= "Xaa at position 60 is Ala or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site

-253-

(D) OTHER INFORMATION: /note= "Xaa at position 87 is Leu, Ser, or Tyr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 88

(D) OTHER INFORMATION: /note= "Xaa at position 88 is Ala or Trp"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 91

(D) OTHER INFORMATION: /note= "Xaa at position 91 is Ala or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 93

(D) OTHER INFORMATION: /note= "Xaa at position 93 is Pro or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 95

(D) OTHER INFORMATION: /note= "Xaa at position 95 is His or Thr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 98

(D) OTHER INFORMATION: /note= "Xaa at position 98 is His, Ile, or Thr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 100

(D) OTHER INFORMATION: /note= "Xaa at position 100 is Lys or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 101

(D) OTHER INFORMATION: /note= "Xaa at position 101 is Asp, Ala, or Met"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 105

(D) OTHER INFORMATION: /note= "Xaa at position 105 is Asn or Glu"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 109

(D) OTHER INFORMATION: /note= "Xaa at position 109 is Arg, Glu, or Leu"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 112

(D) OTHER INFORMATION: /note= "Xaa at position 112 is Thr or Gln"

-255-

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /note= "Met- or Met-Ala may or may not precede the amino acid in position 1"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /note= "Xaa at position 4 is Asn or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /note= "Xaa at position 5 is Met, Ala, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /note= "Xaa at position 6 is Ile, Pro, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /note= "Xaa at position 9 is Ile, Ala, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /note= "Xaa at position 11 is Thr or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /note= "Xaa at position 15 is Gln, Arg, Val, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /note= "Xaa at position 18 is Leu, Ala, Asn, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /note= "Xaa at position 20 is Leu or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 23
- (D) OTHER INFORMATION: /note= "Xaa at position 23 is Phe,

-257-

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 46
- (D) OTHER INFORMATION: /note= "Xaa at position 46 is Ala or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 48
- (D) OTHER INFORMATION: /note= "Xaa at position 48 is Asn, Val, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 49
- (D) OTHER INFORMATION: /note= "Xaa at position 49 is Arg or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 51
- (D) OTHER INFORMATION: /note= "Xaa at position 51 is Val or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 53
- (D) OTHER INFORMATION: /note= "Xaa at position 53 is Ser, Asn, His, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 55
- (D) OTHER INFORMATION: /note= "Xaa at position 55 is Gln or Glu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 59
- (D) OTHER INFORMATION: /note= "Xaa at position 59 is Ala or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 62
- (D) OTHER INFORMATION: /note= "Xaa at position 62 is Ser, Ala, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 65
- (D) OTHER INFORMATION: /note= "Xaa at position 65 is Lys, Arg, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 67
- (D) OTHER INFORMATION: /note= "Xaa at position 67 is Leu, Glu, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 68

-259-

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 95
- (D) OTHER INFORMATION: /note= "Xaa at position 95 is Arg, Glu, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is Thr or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 102
- (D) OTHER INFORMATION: /note= "Xaa at position 102 is Lys, Val, Trp, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 103
- (D) OTHER INFORMATION: /note= "Xaa at position 103 is Thr or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 106
- (D) OTHER INFORMATION: /note= "Xaa at position 106 is Asn, Gln, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 109
- (D) OTHER INFORMATION: /note= "Xaa at position 109 is Ala or Glu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

```

Asn Cys Ser Xaa Xaa Xaa Asp Glu Xaa Ile Xaa His Leu Lys Xaa Pro
1           5           10           15
Pro Xaa Pro Xaa Leu Asp Xaa Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa
20           25           30
Ile Leu Xaa Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa
35           40           45
Xaa Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa Ile Leu
50           55           60
Xaa Asn Xaa Xaa Pro Cys Xaa Pro Xaa Xaa Thr Ala Xaa Pro Xaa Arg
65           70           75           80
Xaa Pro Ile Xaa Ile Xaa Xaa Gly Asp Trp Xaa Glu Phe Arg Xaa Lys
85           90           95
Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln
100          105          110

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(2) INFORMATION FOR SEQ ID NO:9:

-261-

85 90 95
 Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
 100 105 110

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val Pro
 1 5 10 15
 Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp
 20 25 30
 Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn
 35 40 45
 Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu
 50 55 60
 Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg
 65 70 75 80
 His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
 85 90 95
 Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
 100 105 110

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro
 1 5 10 15
 Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp
 20 25 30
 Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe Val
 35 40 45

-263-

Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp
 20 25 30
 Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val
 35 40 45
 Arg Ala Val Lys His Leu Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu
 50 55 60
 Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg
 65 70 75 80
 His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
 85 90 95
 Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
 100 105 110

(2) INFORMATION FOR SEQ ID NO:15:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 111 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro
 1 5 10 15
 Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp
 20 25 30
 Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn
 35 40 45
 Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu
 50 55 60
 Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg
 65 70 75 80
 His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Arg Lys
 85 90 95
 Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
 100 105 110

(2) INFORMATION FOR SEQ ID NO:16:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 111 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

-265-

- (A) LENGTH: 111 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

```

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro
1           5           10           15
Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp
          20           25           30
Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn
          35           40           45
Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu
          50           55           60
Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg
65           70           75           80
His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Glu Lys
          85           90           95
Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln
          100          105          110

```

(2) INFORMATION FOR SEQ ID NO:19:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 111 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

```

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro
1           5           10           15
Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp
          20           25           30
Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn
          35           40           45
Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu
          50           55           60
Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg
65           70           75           80
His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
          85           90           95

```


-267-

Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg
 65 70 75 80
 His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
 85 90 95
 Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln
 100 105 110.

(2) INFORMATION FOR SEQ ID NO:22:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 111 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
 1 5 10 15
 Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp
 20 25 30
 Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val
 35 40 45
 Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu
 50 55 60
 Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg
 65 70 75 80
 His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
 85 90 95
 Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
 100 105 110

(2) INFORMATION FOR SEQ ID NO:23:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 111 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
 1 5 10 15
 Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp
 20 25 30

-269-

```

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys
1           5           10           15
Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
           20           25           30
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala
           35           40           45
Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala
           50           55           60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65           70           75           80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
           85           90           95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
           100          105          110
Gln

```

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

```

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys
1           5           10           15
Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
           20           25           30
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala
           35           40           45
Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala
           50           55           60
Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65           70           75           80
Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
           85           90           95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
           100          105          110
Gln

```

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-271-

Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro
 65 70 75 80
 Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg
 85 90 95
 Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Ile Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Ala Ile Glu Ser
 50 55 60
 Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro
 65 70 75 80
 Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg
 85 90 95
 Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

-273-

(2) INFORMATION FOR SEQ ID NO:32:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 113 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
          20           25           30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
          35           40           45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50           55           60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65           70           75           80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
          85           90           95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
          100          105          110
Gln

```

(2) INFORMATION FOR SEQ ID NO:33:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 113 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp
          20           25           30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala
          35           40           45
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50           55           60

```


-275-

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
 100 105 110
 Gln

-276-

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 113 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp
          20           25           30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala
          35           40           45
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50           55           60
Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65           70           75           80
Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
          85           90           95
Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
          100          105          110
Gln

```

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 113 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
          20           25           30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
          35           40           45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50           55           60

```

-277-

Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp
 20 25 30
 Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

-278-

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp
 20 25 30
 Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Ser Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ala Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30
 Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln

-279-

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
          20           25           30
Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
          35           40           45
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50           55           60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65           70           75           80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
          85           90           95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
          100          105          110
Gln

```

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp
          20           25           30
Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
          35           40           45
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50           55           60

```

-280-

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30
 Val Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

-281-

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30
 Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 125 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Lys Asn Cys
 1 5 10 15
 Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala
 20 25 30
 Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu
 35 40 45
 Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala
 50 55 60
 Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
 65 70 75 80
 Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
 85 90 95
 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
 100 105 110
 Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 115 120 125

-282-

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 125 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

```

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn Cys
1           5           10           15

Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn
          20           25           30

Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
          35           40           45

Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
          50           55           60

Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
65           70           75           80

Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
          85           90           95

Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
          100          105          110

Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          115          120          125

```

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Leu Ile His His Leu Lys
1           5           10           15

Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu Asn Ser Glu Asp
          20           25           30

Val Ser Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
          35           40           45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50           55           60

```

-283-

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 134 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Met Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
 1 5 10 15
 Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro Pro
 20 25 30
 Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp Ile
 35 40 45
 Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg
 50 55 60
 Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys
 65 70 75 80
 Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His
 85 90 95
 Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
 100 105 110
 Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln Thr Thr
 115 120 125
 Leu Ser Leu Ala Ile Phe
 130

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 36 amino acids
- (B) TYPE: amino acid

-284-

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Gly Gly Gly
1 5 10 15
Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser
20 25 30
Gly Gly Gly Ser
35

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Ile Ser Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro
1 5 10 15
Ser Lys Glu Ser His Lys Ser Pro
20

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 28 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

Ile Glu Gly Arg Ile Ser Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
1 5 10 15
Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
20 25

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 906 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

-285-

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTAGG CCCTGCCAGC | 420 |
| TCCCTGCCCC AGAGCTTCCT GCTCAAGTGC TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT | 480 |
| GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG | 540 |
| GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG | 600 |
| GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT CTACCAGGGG | 660 |
| CTCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC CCACCTTGA CACACTGCAG | 720 |
| CTGGACGTCG CCGACTTTGC CACCACCATC TAACTGGGAA TGGCCCCTGC CCTGCAGCCC | 780 |
| ACCCAGGGTG CCATGCCGGC CTTGCCTCT GCTTTCCAGC GCCGGGCAGG AGGGGTCCTG | 840 |
| GTTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGCG | 900 |
| CAGCCC | 906 |

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |

-286-

| | |
|---|-----|
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT | 420 |
| GAAATTATAC ATCACTTAAA GAGACCACCT AACCCTTTGC TGGACCCGAA CAACCTCAAT | 480 |
| TCTGAAGACA TGGATATCCT GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTC | 540 |
| GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC | 600 |
| CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA | 660 |
| GGTGACTGGC AAGAATCCG GGAAAACTG ACGTTCTATC TGGTTACCCT TGAGCAAGCG | 720 |
| CAGGAACAAC AG | 732 |

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

| | |
|--|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCAC CGGCTCGTTC CCCGTCCCCG | 420 |
| TCTACCCAGC CGTGGGAACA CGTGAATGCC ATCCAGGAGG CCCGGCGTCT CCTGAACCTG | 480 |
| AGTAGAGACA CTGCTGCTGA GATGAATGAA ACAGTAGAAG TGATATCAGA AATGTTTGAC | 540 |
| CTCCAGGAGC CGACTTGCCT ACAGACCCGC CTGGAGCTGT ACAAGCAGGG CCTGCGGGGC | 600 |
| AGCCTACCA AGCTCAAGGG CCCCTTGACC ATGATGGCCA GCCACTACAA GCAGCACTGC | 660 |
| CCTCCAACCC CGGAACTTC CTGTGCAACC CAGATTATCA CCTTTGAAAG TTTCAAAGAG | 720 |
| AACCTGAAGG ACTTCCTGCT TGTATCCCC TTTGACTGCT GGGAGCCAGT CCAGGAG | 777 |

-287-

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

| | |
|--|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG GTGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC | 420 |
| TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT | 480 |
| GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG | 540 |
| GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG | 600 |
| GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT CTACCAGGGG | 660 |
| CTCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC CCACCTTGA CACACTGCAG | 720 |
| CTGGACGTCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGAAGAAGT GGAATGGCC | 780 |
| CCTGCCCTGC AGCCCACCCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG | 840 |
| GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT | 900 |
| CTACGCCACC TTGCGCAGCC C | 921 |

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 951 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

-288-

| | |
|--|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTC CAGTACCACC AGGTGAAGAT | 420 |
| TCCAAAGATG TGGCCGCCCC ACACAGACAG CCACTCACCT CTCAGAACG AATTGACAAA | 480 |
| CAAATTCGGT ACATCCTCGA CGGGATATCA GCCCTGAGAA AGGAGACATG TAACAAGAGT | 540 |
| AACATGTGTG AAAGCAGCAA AGAGGCGCTA GCAGAAAACA ACCTGAACCT TCCAAAGATG | 600 |
| GCTGAAAAAG ATGGATGCTT CCAATCCGGA TTCAATGAGG AGACTTGCCT GGTGAAAATC | 660 |
| ATCACTGGTC TTTTGAGGTT TGAGGTATAC CTCGAGTACC TCCAGAACAG ATTTGAGAGT | 720 |
| AGTGAGGAAC AAGCCAGAGC TGTGCAGATG TCGACAAAAG TCCTGATCCA GTTCCTGCAG | 780 |
| AAAAAGGCAA AGAATCTAGA TGCAATAACC ACCCCTGACC CAACCACAAA TGCATCCCTG | 840 |
| CTGACGAAGC TGCAGGCACA GAACCACTGG CTGCAGGACA TGACAACTCA TCTCATTCTG | 900 |
| CGCAGCTTTA AGGAGTTCCT GCAGTCCAGC CTGAGGGCTC TTCGGCAAAT G | 951 |

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

| | |
|--|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT | 420 |

-289-

| | |
|---|-----|
| GAAATTATAC ATCACTTAAA GAGACCACCT AACCCCTTGC TGGACCGAA CAACCTCAAT | 480 |
| TCTGAAGACA TGGATATCCT GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTC | 540 |
| GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC | 600 |
| CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA | 660 |
| GGTGACTGGC AAGAATTCCG GGAAAACTG ACGTTCTATC TGGTTACCCT TGAGCAAGCG | 720 |
| CAGGAACAAC AG | 732 |

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

| | |
|--|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC | 420 |
| TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT | 480 |
| GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG | 540 |
| GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCAGCCAG | 600 |
| GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT CTACCAGGGG | 660 |
| CTCCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGGTC CCACCTTGGA CACACTGCAG | 720 |
| CTGGACGTCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGGAAGAACT GGGAAATGGCC | 780 |
| CCTGCCCTGC AGCCCACCCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG | 840 |
| GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT | 900 |
| CTACGCCACC TTGCGCAGCC C | 921 |

(2) INFORMATION FOR SEQ ID NO:60:

-290-

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC | 360 |
| TCCCCGGGTG GTGGTTCTGG CGCGGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC | 420 |
| TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT | 480 |
| GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG | 540 |
| GTGTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCTCG CCCCAGCCAG | 600 |
| GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT CTACCAGGGG | 660 |
| CTCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC CCACCTTGA CACACTGCAG | 720 |
| CTGGACGTCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGAAGAAGT GGAATGGCC | 780 |
| CCTGCCCTGC AGCCCACCCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG | 840 |
| GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT | 900 |
| CTACGCCACC TTGCGCAGCC C | 921 |

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

| | |
|---|----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
|---|----|

-291-

| | |
|---|-----|
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTGCTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT | 420 |
| GAAATTATAC ATCACTTAAA GAGACCACCT AACCCTTTGC TGGACCCGAA CAACCTCAAT | 480 |
| TCTGAAGACA TGGATATCCT GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTC | 540 |
| GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC | 600 |
| CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA | 660 |
| GGTGACTGGC AAGAATTCCG GGAAAACTG ACGTCTATC TGGTTACCCT TGAGCAAGCG | 720 |
| CAGGAACAAC AG | 732 |

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTGCTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC | 480 |
| TTAAAGAGAC CACCTAACCC TTTGCTGGAC CCGAACAACC TCAATTCTGA AGACATGGAT | 540 |
| ATCCTGATGG AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG | 600 |
| CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC ATGTCTGCCC | 660 |

-292-

TCTGCCACGG CCGCACCCCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA 720
TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG 777

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC 60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC 120
CTTCGAACTC CAAACCTGCT CGCATTTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA 180
GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC 240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATCCGGGA AAAACTGACG 300
TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGATT 360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA 420
TCTCATAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC 480
TTAAAGAGAC CACCTAACCC TTTGCTGGAC CCGAACAACC TCAATTCTGA AGACATGGAT 540
ATCCTGATGG AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG 600
CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC ATGTCTGCCC 660
TCTGCCACGG CCGCACCCCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA 720
TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG 777

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC 60

-293-

| | |
|---|-----|
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTGCTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC | 480 |
| TTAAAGAGAC CACCTAACCC TTTGCTGGAC CCGAACAACC TCAATTCTGA AGACATGGAT | 540 |
| ATCCTGATGG AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG | 600 |
| CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC ATGTCTGCCC | 660 |
| TCTGCCACGG CCGCACCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA | 720 |
| TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG | 777 |

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1047 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTGCTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAGGATT | 360 |
| TCCCCGGGC CTCCTGTCAA TGCTGGCGGC GGCTCTGGTG GTGGTTCTGG TGGCGGCTCT | 420 |
| GAGGGTGGCG GCTCTGAGGG TGGCGGTTCT GAGGGTGGCG GCTCTGAGGG TGGCGGTTCC | 480 |
| GGTGGCGGCT CCGGTTCCGG TGATTTTGAT TATGAAAACA TGGCTACACC ATTGGGCCCT | 540 |
| GCCAGCTCCC TGCCCCAGAG CTTCTGCTC AAGTCTTTAG AGCAAGTGAG GAAGATCCAG | 600 |
| GGCGATGGCG CAGCGCTCCA GGAGAAGCTG TGTGCCACCT ACAAGCTGTG CCACCCCGAG | 660 |

-294-

| | |
|---|------|
| GAGCTGGTGC TGCTCGGACA CTCTCTGGGC ATCCCCCTGGG CTCCCCCTGAG CTCCTGCCCC | 720 |
| AGCCAGGCCC TGCAGCTGGC AGGCTGCTTG AGCCAACCTCC ATAGCGGCCT TTCCTCTAC | 780 |
| CAGGGGCTCC TGCAGGCCCT GGAAGGGATA TCCCCCGAGT TGGGTCCCAC CTTGGACACA | 840 |
| CTGCAGCTGG ACGTCGCCGA CTTTGCCACC ACCATCTGGC AGCAGATGGA AGAACTGGGA | 900 |
| ATGGCCCCCTG CCCTGCAGCC CACCCAGGGT GCCATGCCGG CCTTCGCCTC TGCTTCCAG | 960 |
| CGCCGGGCAG GAGGGGTCCT GGTGCTAGC CATCTGCAGA GCTTCCTGGA GGTGTCGTAC | 1020 |
| CGCGTTCTAC GCCACCTTGC GCAGCCC | 1047 |

(2) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 903 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGC CTCCTGTCAA TGCTGGCGGC GGCTCTGGTG GTGGTTCTGG TGGCGGTCT | 420 |
| GAGGGTGGCG GCTCTGAGGG TGGCGTTCT GAGGGTGGCG GCTCTGAGGG TGGCGGTTC | 480 |
| GGTGGCGGCT CCGGTTCCGG TGATTTTGAT TATGAAAACA TGGCACCGGC TCGTTCCCCG | 540 |
| TCCCCGTCTA CCCAGCCGTG GGAACACGTG AATGCCATCC AGGAGGCCCC GCGTCTCCTG | 600 |
| AACCTGAGTA GAGACACTGC TGCTGAGATG AATGAAACAG TAGAAGTGAT ATCAGAAATG | 660 |
| TTTGACCTCC AGGAGCCGAC TTGCCTACAG ACCCGCCTGG AGCTGTACAA GCAGGGCCTG | 720 |
| CGGGGCAGCC TCACCAAGCT CAAGGGCCCC TTGACCATGA TGGCCAGCCA CTACAAGCAG | 780 |
| CACTGCCCTC CAACCCCGGA AACTTCCTGT GCAACCCAGA TTATCACCTT TGAAAGTTTC | 840 |
| AAAGAGAACC TGAAGGACTT CCTGCTTGTC ATCCCCTTTG ACTGCTGGGA GCCAGTCCAG | 900 |
| GAG | 903 |

-295-

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1017 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

| | |
|---|------|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCCGGTG GCGGCGGCTC TGGTGGTGGT TCTGGTGGCG GCTCTGAGGG TGGCGGCTCT | 420 |
| GAGGGTGGCG GTTCTGAGGG TGGCGGCTCT GAGGGTGGCG GTTCCGGTGG CGGCTCCGGT | 480 |
| TCCGGTAACA TGGCTACACC ATTAGGCCCT GCCAGCTCCC TGCCCCAGAG CTCCTGCTC | 540 |
| AAGTGCTTAG AGCAAGTGAG GAAGATCCAG GGCATGGCG CAGCGCTCCA GGAGAAGCTG | 600 |
| TGTGCCACCT ACAAGCTGTG CCACCCCGAG GAGCTGGTGC TGCTCGGACA CTCTCTGGGC | 660 |
| ATCCCCTGGG CTCCCCTGAG CTCCTGCCCC AGCCAGGCCC TGCAGCTGGC AGGCTGCTTG | 720 |
| AGCCAACTCC ATAGCGGCCT TTTCCTCTAC CAGGGGCTCC TGCAGGCCCT GGAAGGGATA | 780 |
| TCCCCGAGT TGGGTCCAC CTTGGACACA CTGCAGCTGG ACGTCGCCGA CTTTGCCACC | 840 |
| ACCATCTGGC AGCAGATGGA AGAACTGGGA ATGGCCCCTG CCCTGCAGCC CACCCAGGGT | 900 |
| GCCATGCCGG CCTTCGCCTC TGCTTTCCAG CGCCGGGCAG GAGGGGTCCT GGTTGCTAGC | 960 |
| CATCTGCAGA GCTTCTGGA GGTGTCGTAC CGCGTTCTAC GCCACCTGCG GCAGCCC | 1017 |

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

-296-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

| | |
|--|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCCAAACAT GGCTACACCA TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC | 480 |
| TTCTGTCTCA AGTGCTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG | 540 |
| GAGAAGCTGT GTGCCACCTA CAAGCTGTGC CACCCGAGG AGCTGGTGCT GCTCGGACAC | 600 |
| TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT GCAGCTGGCA | 660 |
| GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC AGGGGCTCCT GCAGGCCCTG | 720 |
| GAAGGGATAT CCCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC | 780 |
| TTTGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGGAA TGGCCCCTGC CCTGCAGCCC | 840 |
| ACCCAGGGTG CCATGCCGGC CTTGCTCTCT GCTTTCAGC GCCGGGCAGG AGGGGTCTCTG | 900 |
| GTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGTCTTACC GCGTTCTACG CCACCTTGCG | 960 |
| CAGCCC | 966 |

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 822 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

| | |
|--|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |

-297-

| | |
|---|-----|
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCCAAACAT GGCACCGGCT CGTTCCCCGT CCGCTCTAC CCAGCCGTGG | 480 |
| GAACACGTGA ATGCCATCCA GGAGGCCCCG CGTCTCCTGA ACCTGAGTAG AGACACTGCT | 540 |
| GCTGAGATGA ATGAAACAGT AGAAGTGATA TCAGAAATGT TTGACCTCCA GGAGCCGACT | 600 |
| TGCCTACAGA CCCGCTTGA GCTGTACAAG CAGGGCCTGC GGGGCAGCCT CACCAAGCTC | 660 |
| AAGGGCCCTT TGACCATGAT GGCCAGCCAC TACAAGCAGC ACTGCCCTCC AACCCCGGAA | 720 |
| ACTTCCTGTG CAACCCAGAT TATCACCTTT GAAAGTTTCA AAGAGAACCT GAAGGACTTC | 780 |
| CTGCTTGTCA TCCCCTTTGA CTGCTGGGAG CCAGTCCAGG AG | 822 |

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGATT | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCCAAACAT GGCTACACCA TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC | 480 |
| TTCTGCTCA AGTGCTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG | 540 |
| GAGAAGCTGT GTGCCACCTA CAAGCTGTGC CACCCGAGG AGCTGGTGCT GCTCGGACAC | 600 |
| TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT GCAGCTGGCA | 660 |
| GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC AGGGGCTCCT GCAGGCCCTG | 720 |
| GAAGGGATAT CCCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC | 780 |
| TTTGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGGAA TGGCCCCTGC CCTGCAGCCC | 840 |

-298-

ACCCAGGGTG CCATGCCGGC CTCGCCTCT GCTTTCCAGC GCCGGGCAGG AGGGGTCCTG 900
 GTTGCTAGCC ATCTGCAGAG CTCCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGCG 960
 CAGCCC 966

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic).

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC 60
 CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC 120
 CTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA 180
 GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC 240
 TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG 300
 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC 360
 TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA 420
 TCTCATAAAT CTCCAAACAT GGCTACACCA TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC 480
 TTCCTGCTCA AGTGCTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG 540
 GAGAAGCTGT GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC 600
 TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT GCAGCTGGCA 660
 GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC AGGGGCTCCT GCAGGCCCTG 720
 GAAGGGATAT CCCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC 780
 TTTGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGGAA TGGCCCCTGC CCTGCAGCCC 840
 ACCCAGGGTG CCATGCCGGC CTCGCCTCT GCTTTCCAGC GCCGGGCAGG AGGGGTCCTG 900
 GTTGCTAGCC ATCTGCAGAG CTCCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGCG 960
 CAGCCC 966

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

-299-

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

| | |
|---|-----|
| ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG | 540 |
| GGAAGGATTT CCCCAGGTGG TGGTTCTGGC GGCGGCTCCA ACATGGCTAA CTGCTCTATA | 600 |
| ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTA ACCCTTTGCT GGACCCGAAC | 660 |
| AACCTCAATT CTGAAGACAT GGATATCCTG ATGGAACGAA ACCTTCGAAC TCCAAACCTG | 720 |
| CTCGCATTCT TAAGGGCTGT CAAGCACTTA GAAAATGCAT CAGGTATTGA GGCAATTCTT | 780 |
| CGTAATCTCC AACCATGTCT GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC | 840 |
| ATCAAGGCAG GTGACTGGCA AGAATTCCGG GAAAACTGA CGTTCTATCT GGTTACCCCT | 900 |
| GAGCAAGCGC AGGAACAACA G | 921 |

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 966 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

| | |
|---|-----|
| ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |

-300-

| | |
|---|-----|
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG | 540 |
| GGAAGGATTT CCCCAGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG | 600 |
| TCTAAGAAT CTCATAAATC TCCAAACATG GCTAACTGCT CTATAATGAT CGATGAAATT | 660 |
| ATACATCACT TAAAGAGACC ACCTAACCCCT TTGCTGGACC CGAACACCT CAATTCTGAA | 720 |
| GACATGGATA TCCTGATGGA ACGAAACCTT CGAACTCCAA ACCTGCTCGC ATTCGTAAGG | 780 |
| GCTGTCAAGC ACTTAGAAAA TGCATCAGGT ATTGAGGCAA TTCTTCGTAA TCTCCAACCA | 840 |
| TGTCTGCCCT CTGCCACGGC CGCACCCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC | 900 |
| TGGCAAGAAT TCCGGGAAAA ACTGACGTTT TATCTGGTTA CCCTTGAGCA AGCGCAGGAA | 960 |
| CAACAG | 966 |

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1047 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

| | |
|---|-----|
| ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG | 540 |

-301-

| | |
|--|------|
| GGAAGGATTT CCCCCGGGCC TCCTGTCAAT GCTGGCGGCG GCTCTGGTGG TGGTTCTGGT | 600 |
| GGCGGCTCTG AGGGTGGCGG CTCTGAGGGT GGCGGTTCTG AGGGTGGCGG CTCTGAGGGT | 660 |
| GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT GATTTTGATT ATGAAAACAT GGCTAACTGC | 720 |
| TCTATAATGA TCGATGAAAT TATACATCAC TTAAAGAGAC CACCTAACCC TTTGCTGGAC | 780 |
| CCGAACAACC TCAATTCTGA AGACATGGAT ATCCTGATGG AACGAAACCT TCGAACTCCA | 840 |
| AACCTGCTCG CATTCTGAAG GGCTGTCAAG CACTTAGAAA ATGCATCAGG TATTGAGGCA | 900 |
| ATTCTTCGTA ATCTCCAACC ATGTCTGCCC TCTGCCACGG CCGCACCCCTC TCGACATCCA | 960 |
| ATCATCATCA AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA AACTGACGTT CTATCTGGTT | 1020 |
| ACCCTTGAGC AAGCGCAGGA ACAACAG | 1047 |

(2) INFORMATION FOR SEQ ID NO:75:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 921 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

| | |
|--|-----|
| ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG | 540 |
| GGAAGGATTT CCCC GGGTGG TGGTTCTGGC GGCGGCTCCA ACATGGCTAA CTGCTCTATA | 600 |
| ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTG CACCTTTGCT GGACCCGAAC | 660 |
| AACCTCAATG ACGAAGACGT CTCTATCCTG ATGGAACGAA ACCTTCGACT TCCAAACCTG | 720 |
| GAGAGCTTCG TAAGGGCTGT CAAGAACTTA GAAATGCAT CAGGTATTGA GGCAATTCTT | 780 |
| CGTAATCTCC AACCATGTCT GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC | 840 |

-302-

ATCAAGGCAG GTGACTGGCA AGAATTCCGG GAAAACTGA CGTTCATCT GGTACCCTT 900
 GAGCAAGCGC AGGAACAACA G 921

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1047 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

ATGGCTACAC CATTAGGCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA 60
 GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC 120
 TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG 180
 GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC 240
 CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCGAG 300
 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG 360
 CAGCAGATGG AAGAACTGGG AATGGCCCTT GCCCTGCAGC CCACCCAGGG TGCCATGCCG 420
 GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGTCC TGGTTGCTAG CCATCTGCAG 480
 AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG 540
 GGAAGGATTT CCCCCGGGCC TCCTGTCAAT GCTGGCGGCG GCTCTGGTGG TGGTTCTGGT 600
 GGCGGCTCTG AGGGTGGCGG CTCTGAGGGT GGCGGTTCTG AGGGTGGCGG CTCTGAGGGT 660
 GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT GATTTTGATT ATGAAAACAT GGCTAACTGC 720
 TCTATAATGA TCGATGAAAT TATACATCAC TTAAAGAGAC CACCTGCACC TTTGCTGGAC 780
 CCGAACAACC TCAATGACGA AGACGTCTCT ATCCTGATGG AACGAAACCT TCGACTTCCA 840
 AACCTGGAGA GCTTCGTAAG GGCTGTCAAG AACTTAGAAA ATGCATCAGG TATTGAGGCA 900
 ATTCTTCGTA ATCTCCAACC ATGTCTGCCC TCTGCCACGG CCGCACCTC TCGACATCCA 960
 ATCATCATCA AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA AACTGACGTT CTATCTGGTT 1020
 ACCCTTGAGC AAGCGCAGGA ACAACAG 1047

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

-303-

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

| | |
|---|-----|
| ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG | 540 |
| GGAAGGATTT CCCCGGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG | 600 |
| TCTAAAGAAT CTCATAAATC TCCAAACATG GCTAACTGCT CTATAATGAT CGATGAAATT | 660 |
| ATACATCACT TAAAGAGACC ACCTGCACCT TTGCTGGACC CGAACAACCT CAATGACGAA | 720 |
| GACGTCTCTA TCCTGATGGA ACGAAACCTT CGACTTCCAA ACCTGGAGAG CTTGTAAGG | 780 |
| GCTGTCAAGA ACTTAGAAAA TGCATCAGGT ATTGAGGCAA TTCTTCGTAA TCTCCAACCA | 840 |
| TGTCTGCCCT CTGCCACGGC CGCACCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC | 900 |
| TGGCAAGAAT TCCGGGAAAA ACTGACGTTT TATCTGGTTA CCCTTGAGCA AGCGCAGGAA | 960 |
| CAACAG | 966 |

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

| | |
|---|-----|
| ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |

-304-

| | |
|---|-----|
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC | 540 |
| GGTGGAGGCT CCCCAGGTGG TGGTTCTGGC GCGCGCTCCA ACATGGCTAA CTGCTCTATA | 600 |
| ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTG CACCTTTGCT GGACCCGAAC | 660 |
| AACCTCAATG ACGAAGACGT CTCTATCCTG ATGGAACGAA ACCTTCGACT TCCAAACCTG | 720 |
| GAGAGCTTCG TAAGGGCTGT CAAGAACTTA GAAAATGCAT CAGGTATTGA GGCAATTCTT | 780 |
| CGTAATCTCC AACCATGTCT GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC | 840 |
| ATCAAGGCAG GTGACTGGCA AGAATTCCGG GAAAACTGA CGTTCTATCT GGTACCCTT | 900 |
| GAGCAAGCGC AGGAACAACA G | 921 |

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

| | |
|---|-----|
| ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC | 540 |

-305-

| | |
|---|-----|
| GGTGGAGGCT CCCCAGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG | 600 |
| TCTAAGAAT CTCATAAATC TCCAAACATG GCTAACTGCT CTATAATGAT CGATGAAATT | 660 |
| ATACATCACT TAAAGAGACC ACCTGCACCT TTGCTGGACC CGAACAACCT CAATGACGAA | 720 |
| GACGTCTCTA TCCTGATGGA ACGAAACCTT CGACTTCCAA ACCTGGAGAG CTTGTAAGG | 780 |
| GCTGTCAAGA ACTTAGAAAA TGCATCAGGT ATTGAGGCAA TTCTTCGTAA TCTCCAACCA | 840 |
| TGTCTGCCCT CTGCCACGGC CGCACCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC | 900 |
| TGGCAAGAAT TCCGGGAAAA ACTGACGTTT TATCTGGTTA CCCTTGAGCA AGCGCAGGAA | 960 |
| CAACAG | 966 |

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

| | |
|---|-----|
| ATGGCTACAC CATTGGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTCTTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| GAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC | 540 |
| GGTGGAGGCT CCCCAGGTGG TGGTTCTGGC GCGGGCTCCA ACATGGCTAA CTGCTCTATA | 600 |
| ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTG CACCTTTGCT GGACCCGAAC | 660 |
| AACCTCAATG ACGAAGACGT CTCTATCCTG ATGGAACGAA ACCTTCGACT TCCAAACCTG | 720 |
| GAGAGCTTCG TAAGGGCTGT CAAGAACTTA GAAAATGCAT CAGGTATTGA GGCAATTCTT | 780 |
| CGTAATCTCC AACCATGTCT GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC | 840 |
| ATCAAGGCAG GTGACTGGCA AGAATTCCGG GAAAACTGA CGTCTATCT GGTTACCCTT | 900 |

-306-

GAGCAAGCGC AGGAACAACA G

921

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

| | |
|---|-----|
| ATGGCTACAC CATTGGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTCTTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC | 540 |
| GGTGGAGGCT CCCCAGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG | 600 |
| TCTAAAGAAT CTCATAAATC TCCAAACATG GCTAACTGCT CTATAATGAT CGATGAAATT | 660 |
| ATACATCACT TAAAGAGACC ACCTGCACCT TTGCTGGACC CGAACAACCT CAATGACGAA | 720 |
| GACGTCTCTA TCCTGATGGA ACGAAACCTT CGACTTCCAA ACCTGGAGAG CTCGTAAGG | 780 |
| GCTGTCAAGA ACTTAGAAAA TGCATCAGGT ATTGAGGCAA TTCTTCGTAA TCTCCAACCA | 840 |
| TGTCTGCCCT CTGCCACGGC CGCACCCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC | 900 |
| TGGCAAGAAT TCCGGGAAAA ACTGACGTTT TATCTGGTTA CCCTTGAGCA AGCGCAGGAA | 960 |
| CAACAG | 966 |

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

-307-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC | 120 |
| CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC | 480 |
| TTAAAGAGAC CACCTGCACC TTTGCTGGAC CCGAACAACC TCAATGACGA AGACGTCTCT | 540 |
| ATCCTGATGG AACGAAACCT TCGACTTCCA AACCTGGAGA GCTTCGTAAG GGCTGTCAAG | 600 |
| AACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC ATGTCTGCCC | 660 |
| TCTGCCACGG CCGCACCTTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA | 720 |
| TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG | 777 |

(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 984 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC | 120 |
| CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCCAAACAT GGCTACACCA TTGGGCCCTG CCAGCTCCCT GCCCCAGAGC | 480 |

-308-

| | |
|---|-----|
| TTCCTGCTCA AGTCTTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG | 540 |
| GAGAAGCTGT GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC | 600 |
| TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT GCAGCTGGCA | 660 |
| GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC AGGGGCTCCT GCAGGCCCTG | 720 |
| GAAGGGATAT CCCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC | 780 |
| TTTGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGGAA TGGCCCCTGC CCTGCAGCCC | 840 |
| ACCCAGGGTG CCATGCCGGC CTTGCGCTCT GCTTTCCAGC GCCGGGCAGG AGGGGTCCTG | 900 |
| GTTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGCG | 960 |
| CAGCCCTGAT AAGGATCCGA ATTC | 984 |

(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC | 120 |
| CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTAGG CCCTGCCAGC | 420 |
| TCCCTGCCCC AGAGCTTCCT GCTCAAGTGC TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT | 480 |
| GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG | 540 |
| GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG | 600 |
| GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT CTACCAGGGG | 660 |
| CTCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC CCACCTTGGA CACTGCAG | 720 |
| CTGGACGTCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGGAAGAACT GGAATGGCC | 780 |
| CCTGCCCTGC AGCCACCCA GGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG | 840 |

-309-

GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT 900
 CTACGCCACC TTGCGCAGCC C 921

(2) INFORMATION FOR SEQ ID NO:85:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 921 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA 60
 CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC 120
 CTTGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA 180
 GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC 240
 TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGA AAAACTGACG 300
 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAGGATT 360
 TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC 420
 TCCCTGCCCC AGAGCTTCTT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT 480
 GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG 540
 GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCAGCCAG 600
 GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCATAGCG GCCTTTTCTT CTACCAGGGG 660
 CTCCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGGTC CCACCTTGA CACTGCAG 720
 CTGGACGTCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGAAGAAGT GGAATGGCC 780
 CCTGCCCTGC AGCCACCCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG 840
 GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT 900
 CTACGCCACC TTGCGCAGCC C 921

(2) INFORMATION FOR SEQ ID NO:86:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 732 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

-310-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC | 120 |
| CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAGGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT | 420 |
| GAAATTATAC ATCACTTAAA GAGACCACCT GCACCTTTGC TGGACCCGAA CAACCTCAAT | 480 |
| GACGAAGACG TCTCTATCCT GATGGAACGA AACCTTCGAC TTCCAAACCT GGAGAGCTTC | 540 |
| GTAAGGGCTG TCAAGAACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC | 600 |
| CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA | 660 |
| GGTGACTGGC AAGAATTCCG GGAAAACTG ACGTTCTATC TGGTTACCCT TGAGCAAGCG | 720 |
| CAGGAACAAC AG | 732 |

(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC | 120 |
| CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC | 420 |
| TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT | 480 |

-311-

| | |
|--|-----|
| GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG | 540 |
| GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG | 600 |
| GCCCTGCAGC TGGCAGGCTG CTGAGCCAA CTCCATAGCG GCCTTTTCCT CTACCAGGGG | 660 |
| CTCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC CCACCTTGGA CACACTGCAG | 720 |
| CTGGACGTCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGGAAGAACT GGGAAATGGCC | 780 |
| CCTGCCCTGC AGCCACCCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG | 840 |
| GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT | 900 |
| CTACGCCACC TTGCGCAGCC C | 921 |

(2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC | 120 |
| CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT | 420 |
| GAAATTATAC ATCACTTAAA GAGACCACCT GCACCTTTGC TGGACCCGAA CAACCTCAAT | 480 |
| GACGAAGACG TCTCTATCCT GATGGAACGA AACCTTCGAC TTCCAAACCT GGAGAGCTTC | 540 |
| GTAAGGGCTG TCAAGAACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC | 600 |
| CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA | 660 |
| GGTGACTGGC AAGAATTCCG GGAAAACTG ACGTTCTATC TGGTTACCCT TGAGCAAGCG | 720 |
| CAGGAACAAC AG | 732 |

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs

-312-

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC | 120 |
| CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCAAACAT GGCTACACCA TTGGGCCCTG CCAGCTCCCT GCCCCAGAGC | 480 |
| TTCTGCTCA AGTCTTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG | 540 |
| GAGAAGCTGT GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC | 600 |
| TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT GCAGCTGGCA | 660 |
| GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC AGGGGCTCCT GCAGGCCCTG | 720 |
| GAAGGGATAT CCCCCGAGT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC | 780 |
| TTTGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGGAA TGGCCCCTGC CCTGCAGCCC | 840 |
| ACCCAGGGTG CCATGCCGGC CTTGCCTCT GCTTTCCAGC GCCGGGCAGG AGGGGTCCTG | 900 |
| GTTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGTGCTACC GCGTTCTACG CCACCTTGCG | 960 |
| CAGCCC | 966 |

(2) INFORMATION FOR SEQ ID NO:90:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 777 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

| | |
|---|----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA | 60 |
|---|----|

-313-

| | |
|--|-----|
| CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC | 120 |
| CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATCCCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC | 360 |
| TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA | 420 |
| TCTCATAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC | 480 |
| TTAAAGAGAC CACCTGCACC TTTGCTGGAC CCGAACAAACC TCAATGACGA AGACGTCTCT | 540 |
| ATCCTGATGG AACGAAACCT TCGACTTCCA AACCTGGAGA GCTTCGTAAG GGCTGTCAAG | 600 |
| AACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC ATGTCTGCCC | 660 |
| TCTGCCACGG CCGCACCCCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA | 720 |
| TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG | 777 |

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 41 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

AATTCGGGA AAAACTGACG TTCTATCTGG TTACCCTTGA G

41

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 46 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

CTGCGCTTGC TCAAGGGTAA CCAGATAGAA CGTCAGTTTT TCCCGG

46

(2) INFORMATION FOR SEQ ID NO:93:

-314-

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

CAAGCGCAGG AACACAGTA CGTAATCGAG GGAAGGATT

39

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

ACCCGGGGAA ATCCTTCCCT CGATTACGTA CTGTTGTTC

39

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 63 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

TCCCCGGGTG GTGTTTCTGG CGGCGGCTCC AACATGTAAG GTACCGCATG CAAGCTTAGA

60

TCT

63

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 58 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

-315-

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

AGCTAGATCT AAGCTTGCAT GCGGTACCTT ACATGTTGGA GCCGCCGCCA GAACCACC 58

(2) INFORMATION FOR SEQ ID NO:97:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 74 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

CCGGGTGAAC CGTCTGGTCC AATCTCTACT ATCAACCCGT CTCCTCCGTC TAAAGAATCT 60
CATAAATCTC CAAA 74

(2) INFORMATION FOR SEQ ID NO:98:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 74 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

CATGTTTGGA GATTATGAG ATTCTTTAGA CGGAGGAGAC GGGTTGATAG TAGAGATTGG 60
ACCAGACGGT TCAC 74

(2) INFORMATION FOR SEQ ID NO:99:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 68 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

-316-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

CTAGCCATCT GCAGAGCTTC CTGGAGGTGT CGTACCGCGT TCTACGCCAC CTTGCGCAGC 60
CCTACGTA 68

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 68 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

AGCTTACGTA GGGCTGCGCA AGGTGGCGTA GAACGCGGTA CGACACCTCC AGGAAGCTCT 60
GCAGATGG 68

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

GTAATCGAGG GAAAGATTTC C 21

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

-317-

CCGGGGAAAT CTTCCCTCG ATTAC

25

(2) INFORMATION FOR SEQ ID NO:103:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 21 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

GTAGAGGGCG GTGGAGGCTC C

21

(2) INFORMATION FOR SEQ ID NO:104:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

CCGGGGAGCC TCCACGCCC TCTAC

25

(2) INFORMATION FOR SEQ ID NO:105:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 58 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "sythetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

CATGGCACCA GCAAGATCAC CATCACCATC AACTCAACCT TGGGAACATG TGAATGCC

58

(2) INFORMATION FOR SEQ ID NO:106:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 52 base pairs
 - (B) TYPE: nucleic acid

-318-

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

CATTACATG TTCCCAAGGT TGAGTTGATG GTGATGGTGA TCTTGCTGGT GC

52

(2) INFORMATION FOR SEQ ID NO:107:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 66 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

CTGCCAGCTC CCTGCCCCAG AGCTTCCTGC TCAAGTCTTT AGAGCAAGTG AGGAAGATCC

60

AGGGCG

66

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 66 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

CTGGATCTTC CTCATTGCT CTAAAGACTT GAGCAGGAAG CTCTGGGGCA GGGAGCTGGC

60

AGGGCC

66

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 48 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

-319-

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

AGCTTACCTG CCATGGCTCC AGTACCACCA GGTGAAGATT CCAAAGAT

48

- (2) INFORMATION FOR SEQ ID NO:110:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 40 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

TTGGAATCTT CACCTGGTGG TACTGGAGCC ATGGCAGGTA

40

- (2) INFORMATION FOR SEQ ID NO:111:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

AGCTTCCATG GCTACCCCCC TGGGCC

26

- (2) INFORMATION FOR SEQ ID NO:112:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 18 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

-320-

CAGGGGGGTA GCCATGGA

18

(2) INFORMATION FOR SEQ ID NO:113:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:

CATGGCTACA CCATTGGGCC

20

(2) INFORMATION FOR SEQ ID NO:114:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:

CAATGGTGTA GC

12

(2) INFORMATION FOR SEQ ID NO:115:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

CATGGCTACA CCATTAGGAC

20

(2) INFORMATION FOR SEQ ID NO:116:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 base pairs
- (B) TYPE: nucleic acid

-321-

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:

TAATGGTGTA GC

12

- (2) INFORMATION FOR SEQ ID NO:117:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

CCTGTCAACC CGGGCGGCGG CTCTGGTGGT

30

- (2) INFORMATION FOR SEQ ID NO:118:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:

TCATAATACA TGTTACCGGA ACGGAGCCGC C

31

- (2) INFORMATION FOR SEQ ID NO:119:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 34 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

-322-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

ATCGTCTGAC CTCCCGGGAC CTCCTGTCAA TGCT

34

(2) INFORMATION FOR SEQ ID NO:120:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

AGCGTTTGAC ATGTTTTTCAT AATCAAAATC

30

(2) INFORMATION FOR SEQ ID NO:121:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly
115 120 125

-323-

Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 130 135 140
 Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
 145 150 155 160
 Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
 165 170 175
 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
 180 185 190
 Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
 195 200 205
 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
 210 215 220
 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
 225 230 235 240
 Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
 245 250 255
 Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
 260 265 270
 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
 275 280 285
 His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
 290 295 300
 Ala Gln Pro
 305

(2) INFORMATION FOR SEQ ID NO:122:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala

-324-

| | | | | |
|---|-----|----|-----|---------|
| 50 | | 55 | | 60 |
| Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro | | | | |
| 65 | | 70 | | 75 80 |
| Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg | | | | |
| | 85 | | 90 | 95 |
| Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln | | | | |
| | 100 | | 105 | 110 |
| Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly | | | | |
| | 115 | | 120 | 125 |
| Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln | | | | |
| | 130 | | 135 | 140 |
| Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp | | | | |
| | 145 | | 150 | 155 160 |
| Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His | | | | |
| | 165 | | 170 | 175 |
| Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala | | | | |
| | 180 | | 185 | 190 |
| Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu | | | | |
| | 195 | | 200 | 205 |
| Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala | | | | |
| | 210 | | 215 | 220 |
| Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln | | | | |
| | 225 | | 230 | 235 240 |
| Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu | | | | |
| | 245 | | 250 | 255 |
| Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala | | | | |
| | 260 | | 265 | 270 |
| Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser | | | | |
| | 275 | | 280 | 285 |
| His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu | | | | |
| | 290 | | 295 | 300 |
| Ala Gln Pro | | | | |
| 305 | | | | |

(2) INFORMATION FOR SEQ ID NO:123:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

-325-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 130 135 140
 Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
 145 150 155 160
 Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
 165 170 175
 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
 180 185 190
 Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
 195 200 205
 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
 210 215 220
 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
 225 230 235 240
 Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
 245 250 255
 Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
 260 265 270
 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
 275 280 285
 His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
 290 295 300
 Ala Gln Pro

-326-

305

(2) INFORMATION FOR SEQ ID NO:124:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1             5             10             15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20             25             30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35             40             45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50             55             60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65             70             75             80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85             90             95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100             105             110

Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly
115             120             125

Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
130             135             140

Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
145             150             155             160

Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
165             170             175

Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
180             185             190

Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
195             200             205

Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
210             215             220

Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
225             230             235             240

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-327-

Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
 245 250 255

Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
 260 265 270

Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
 275 280 285

His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
 290 295 300

Ala Gln Pro
 305

(2) INFORMATION FOR SEQ ID NO:125:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 244 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly
 115 120 125

Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
 130 135 140

His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
 145 150 155 160

Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn

-328-

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165              170              175
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly
180              185              190
Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
195              200              205
Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
210              215              220
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala
225              230              235              240
Gln Glu Gln Gln

```

(2) INFORMATION FOR SEQ ID NO:126:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 244 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1              5              10              15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20              25              30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35              40              45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50              55              60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65              70              75              80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85              90              95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100             105             110
Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Gly Ser Gly Gly
115             120             125
Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
130             135             140
His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
145             150             155             160

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-329-

Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
 165 170 175
 Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly
 180 185 190
 Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
 195 200 205
 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
 210 215 220
 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala
 225 230 235 240
 Gln Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:127:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 244 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
 130 135 140
 His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn

-330-

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 145 | | 150 | | 155 | | 160 | | | | | | | | | |
| Ser | Glu | Asp | Met | Asp | Ile | Leu | Met | Glu | Arg | Asn | Leu | Arg | Thr | Pro | Asn |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Leu | Leu | Ala | Phe | Val | Arg | Ala | Val | Lys | His | Leu | Glu | Asn | Ala | Ser | Gly |
| | | | 180 | | | | | 185 | | | | | 190 | | |
| Ile | Glu | Ala | Ile | Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| Ala | Ala | Pro | Ser | Arg | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Glu | Phe | Arg | Glu | Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala |
| 225 | | | | | 230 | | | | | 235 | | | | 240 | |
| Gln | Glu | Gln | Gln | | | | | | | | | | | | |

(2) INFORMATION FOR SEQ ID NO:128:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Asn | Cys | Ser | Ile | Met | Ile | Asp | Glu | Ile | Ile | His | His | Leu | Lys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Arg | Pro | Pro | Asn | Pro | Leu | Leu | Asp | Pro | Asn | Asn | Leu | Asn | Ser | Glu | Asp |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Met | Asp | Ile | Leu | Met | Glu | Arg | Asn | Leu | Arg | Thr | Pro | Asn | Leu | Leu | Ala |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Phe | Val | Arg | Ala | Val | Lys | His | Leu | Glu | Asn | Ala | Ser | Gly | Ile | Glu | Ala |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Ile | Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala | Ala | Pro |
| 65 | | | | 70 | | | | | 75 | | | | | 80 | |
| Ser | Arg | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu | Phe | Arg |
| | | | 85 | | | | | 90 | | | | | 95 | | |
| Glu | Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln | Glu | Gln |
| | | 100 | | | | | | 105 | | | | | 110 | | |
| Gln | Tyr | Val | Ile | Glu | Gly | Arg | Ile | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro |
| | 115 | | | | | | 120 | | | | | 125 | | | |
| Ile | Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser |
| 130 | | | | | 135 | | | | | | 140 | | | | |

-331-

Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
 145 150 155 160
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
 165 170 175
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
 180 185 190
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
 195 200 205
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
 210 215 220
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
 225 230 235 240
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
 245 250 255
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
 260 265 270
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
 275 280 285
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His
 290 295 300
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
 305 310 315 320
 Gln Pro

(2) INFORMATION FOR SEQ ID NO:129:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala

-332-

| 50 | 55 | 60 |
|--|----|----|
| Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80 | | |
| Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95 | | |
| Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110 | | |
| Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Glu Pro Ser Gly Pro
115 120 125 | | |
| Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
130 135 140 | | |
| Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
145 150 155 160 | | |
| Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
165 170 175 | | |
| Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
180 185 190 | | |
| Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
195 200 205 | | |
| Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
210 215 220 | | |
| Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
225 230 235 240 | | |
| Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
245 250 255 | | |
| Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
260 265 270 | | |
| Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
275 280 285 | | |
| Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His
290 295 300 | | |
| Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
305 310 315 320 | | |
| Gln Pro | | |

(2) INFORMATION FOR SEQ ID NO:130:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

-333-

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
          20           25           30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
          35           40           45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50           55           60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65           70           75           80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
          85           90           95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
          100          105          110
Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
          115          120          125
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
          130          135          140
Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
          145          150          155          160
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
          165          170          175
Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
          180          185          190
Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
          195          200          205
Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
          210          215          220
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
          225          230          235          240
Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
          245          250          255
Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
          260          265          270
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
          275          280          285

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-334-

Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His
 290 295 300

Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
 305 310 315 320

Gln Pro

(2) INFORMATION FOR SEQ ID NO:131:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125

Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140

Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 145 150 155 160

Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
 165 170 175

Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu
 180 185 190

Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile

-335-

| | | |
|---|-----|-----|
| 195 | 200 | 205 |
| Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala | | |
| 210 | 215 | 220 |
| Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu | | |
| 225 | 230 | 235 |
| Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln | | |
| 245 | 250 | 255 |
| Glu Gln Gln | | |

(2) INFORMATION FOR SEQ ID NO:132:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Asn | Cys | Ser | Ile | Met | Ile | Asp | Glu | Ile | Ile | His | His | Leu | Lys |
| 1 | | | 5 | | | | | 10 | | | | | | 15 | |
| Arg | Pro | Pro | Asn | Pro | Leu | Leu | Asp | Pro | Asn | Asn | Leu | Asn | Ser | Glu | Asp |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Met | Asp | Ile | Leu | Met | Glu | Arg | Asn | Leu | Arg | Thr | Pro | Asn | Leu | Leu | Ala |
| | 35 | | | | | 40 | | | | | | 45 | | | |
| Phe | Val | Arg | Ala | Val | Lys | His | Leu | Glu | Asn | Ala | Ser | Gly | Ile | Glu | Ala |
| 50 | | | | | 55 | | | | | 60 | | | | | |
| Ile | Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala | Ala | Pro |
| 65 | | | 70 | | | | | | 75 | | | | | 80 | |
| Ser | Arg | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu | Phe | Arg |
| | | | 85 | | | | | | 90 | | | | | 95 | |
| Glu | Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln | Glu | Gln |
| | 100 | | | | | | | 105 | | | | | 110 | | |
| Gln | Tyr | Val | Ile | Glu | Gly | Lys | Ile | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro |
| | 115 | | | | | 120 | | | | | | 125 | | | |
| Ile | Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Pro | Asn | Met | Ala | Asn | Cys | Ser | Ile | Met | Ile | Asp | Glu | Ile | Ile | His | His |
| 145 | | | | 150 | | | | | | 155 | | | | 160 | |
| Leu | Lys | Arg | Pro | Pro | Asn | Pro | Leu | Leu | Asp | Pro | Asn | Asn | Leu | Asn | Ser |
| | | | 165 | | | | | | 170 | | | | | 175 | |

-336-

Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu
 180 185 190
 Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile
 195 200 205
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 210 215 220
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 225 230 235 240
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 245 250 255
 Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:133:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His

[illegible]

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Asn | Cys | Ser | Ile | Met | Ile | Asp | Glu | Ile | Ile | His | His | Leu | Lys |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Arg | Pro | Pro | Ala | Pro | Leu | Leu | Asp | Pro | Asn | Asn | Leu | Asn | Asp | Glu | Asp |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Val | Ser | Ile | Leu | Met | Asp | Arg | Asn | Leu | Arg | Leu | Pro | Asn | Leu | Glu | Ser |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Phe | Val | Arg | Ala | Val | Lys | Asn | Leu | Glu | Asn | Ala | Ser | Gly | Ile | Glu | Ala |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Ile | Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala | Ala | Pro |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| Ser | Arg | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu | Phe | Arg |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Glu | Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln | Glu | Gln |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Gln | Tyr | Val | Ile | Glu | Gly | Arg | Ile | Ser | Pro | Gly | Gly | Gly | Ser | Gly | Gly |
| | | 115 | | | | | 120 | | | | | 125 | | | |

-338-

Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 130 135 140
 Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
 145 150 155 160
 Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
 165 170 175
 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
 180 185 190
 Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
 195 200 205
 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
 210 215 220
 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
 225 230 235 240
 Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
 245 250 255
 Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
 260 265 270
 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
 275 280 285
 His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
 290 295 300
 Ala Gln Pro
 305

(2) INFORMATION FOR SEQ ID NO:135:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30
 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala

-339-

| | | |
|---|-----|---------|
| 50 | 55 | 60 |
| Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro | | |
| 65 | 70 | 75 80 |
| Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg | | |
| | 85 | 90 95 |
| Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln | | |
| | 100 | 105 110 |
| Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly | | |
| | 115 | 120 125 |
| Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Leu Pro Gln | | |
| | 130 | 135 140 |
| Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp | | |
| 145 | 150 | 155 160 |
| Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His | | |
| | 165 | 170 175 |
| Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala | | |
| | 180 | 185 190 |
| Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu | | |
| | 195 | 200 205 |
| Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala | | |
| | 210 | 215 220 |
| Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln | | |
| 225 | 230 | 235 240 |
| Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu | | |
| | 245 | 250 255 |
| Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala | | |
| | 260 | 265 270 |
| Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser | | |
| | 275 | 280 285 |
| His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu | | |
| | 290 | 295 300 |
| Ala Gln Pro | | |
| 305 | | |

(2) INFORMATION FOR SEQ ID NO:136:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 244 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

-340-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1           5           10           15
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
          20           25           30
Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
      35           40           45
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50           55           60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65           70           75           80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
          85           90           95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
          100          105          110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly
      115          120          125
Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
      130          135          140
His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
      145          150          155          160
Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn
          165          170          175
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly
          180          185          190
Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
      195          200          205
Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
      210          215          220
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala
      225          230          235          240
Gln Glu Gln Gln

```

(2) INFORMATION FOR SEQ ID NO:137:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

-341-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30
 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 145 150 155 160
 Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
 165 170 175
 Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu
 180 185 190
 Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
 195 200 205
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 210 215 220
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 225 230 235 240
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 245 250 255
 Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:138:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:

-342-

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
20           25           30
Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
35           40           45
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
50           55           60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65           70           75           80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85           90           95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100          105          110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro
115          120          125
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
130          135          140
Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
145          150          155          160
Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
165          170          175
Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
180          185          190
Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
195          200          205
Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
210          215          220
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
225          230          235          240
Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
245          250          255
Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
260          265          270
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe

```


-343-

275 280 285

Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His
290 295 300

Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
305 310 315 320

Gln Pro

(2) INFORMATION FOR SEQ ID NO:139:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 349 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val Asn Ala
115 120 125

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Gly Gly Gly
130 135 140

Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser
145 150 155 160

Gly Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn Met Ala Thr
165 170 175

Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser
180 185 190

-344-

Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu
 195 200 205
 Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
 210 215 220
 Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro
 225 230 235 240
 Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly
 245 250 255
 Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro
 260 265 270
 Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe
 275 280 285
 Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala
 290 295 300
 Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln
 305 310 315 320
 Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
 325 330 335
 Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 340 345

(2) INFORMATION FOR SEQ ID NO:140:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 64 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

GGATCCACCA TGAGCCGCCT GCCCGTCCTG CTCCTGCTCC AACTCCTGGT CCGCCCCGCC 60
 ATGG 64

(2) INFORMATION FOR SEQ ID NO:141:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

-345-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly
 115 120 125

Gly Ser Asn Met Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro
 130 135 140

Trp Glu His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu
 145 150 155 160

Ser Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser
 165 170 175

Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu
 180 185 190

Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro
 195 200 205

Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro
 210 215 220

Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu
 225 230 235 240

Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro
 245 250 255

Val Gln Glu

(2) INFORMATION FOR SEQ ID NO:142:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 301 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

-346-

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1      5      10      15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20      25      30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35      40      45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50      55      60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65      70      75      80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85      90      95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100     105     110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val Asn Ala
115     120     125
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Gly Gly Gly
130     135     140
Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser
145     150     155     160
Gly Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn Met Ala Pro
165     170     175
Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala
180     185     190
Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala
195     200     205
Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln
210     215     220
Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln Gly Leu
225     230     235     240
Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met Met Ala Ser
245     250     255
His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser Cys Ala Thr
260     265     270
Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu
275     280     285

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-347-

Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu
 290 295 300

(2) INFORMATION FOR SEQ ID NO:143:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 335 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Pro Val Asn Ala Gly Gly Gly Ser Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly
 130 135 140

Gly Ser Glu Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Gly Asn Met
 145 150 155 160

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 165 170 175

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
 180 185 190

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
 195 200 205

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
 210 215 220

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His

-348-

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225          230          235          240
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
          245          250          255
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
          260          265          270
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          275          280          285
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
          290          295          300
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
305          310          315          320
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
          325          330          335

```

(2) INFORMATION FOR SEQ ID NO:144:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 274 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1          5          10          15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
          20          25          30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
          35          40          45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
          50          55          60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65          70          75          80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
          85          90          95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
          100          105          110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro
          115          120          125
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
          130          135          140

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-349-

Pro Asn Met Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp
 145 150 155 160

Glu His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser
 165 170 175

Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu
 180 185 190

Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu
 195 200 205

Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu
 210 215 220

Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu
 225 230 235 240

Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn
 245 250 255

Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val
 260 265 270

Gln Glu

(2) INFORMATION FOR SEQ ID NO:145:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 317 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:145:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln

-350-

100 105 110
 Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Ser Asn Met Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val
 130 135 140
 Ala Ala Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys
 145 150 155 160
 Gln Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr
 165 170 175
 Cys Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu
 180 185 190
 Asn Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln
 195 200 205
 Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu
 210 215 220
 Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser
 225 230 235 240
 Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile
 245 250 255
 Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro
 260 265 270
 Asp Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn
 275 280 285
 Gln Trp Leu Gln Asp Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys
 290 295 300
 Glu Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg Gln Met
 305 310 315

(2) INFORMATION FOR SEQ ID NO:146:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:146:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15
 Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30

-351-

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
 35 40 45
 Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60
 Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
 65 70 75 80
 His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95
 Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110
 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125
 Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140
 Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160
 Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175
 Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly
 180 185 190
 Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 195 200 205
 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
 210 215 220
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu
 225 230 235 240
 Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile
 245 250 255
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 260 265 270
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 275 280 285
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 290 295 300
 Glu Gln Gln
 305

(2) INFORMATION FOR SEQ ID NO:147:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

-352-

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:147:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15
 Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30
 Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
 35 40 45
 Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60
 Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
 65 70 75 80
 His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95
 Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110
 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125
 Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140
 Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160
 Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175
 Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly
 180 185 190
 Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 195 200 205
 Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
 210 215 220
 Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu
 225 230 235 240
 Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
 245 250 255
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 260 265 270
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 275 280 285

-353-

Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 290 295 300

Glu Gln Gln
 305

(2) INFORMATION FOR SEQ ID NO:148:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 337 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15

Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
 35 40 45

Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60

Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
 65 70 75 80

His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95

Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

Tyr Val Pro Gln Pro Pro Val Asn Ala Gly Gly Gly Ser Gly Gly Gly
 180 185 190

Ser Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu
 195 200 205

Gly Gly Gly Ser Glu Gly Gly Gly Ser Gly Gly Gly Ser Gly

-354-

210 215 220
 Asp Phe Asp Tyr Glu Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu
 225 230 235 240
 Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn
 245 250 255
 Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
 260 265 270
 Leu Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 275 280 285
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 290 295 300
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 305 310 315 320
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 325 330 335
 Gln

(2) INFORMATION FOR SEQ ID NO:149:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15
 Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30
 Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
 35 40 45
 Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60
 Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
 65 70 75 80
 His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95
 Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110

-355-

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile
 180 185 190

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
 195 200 205

Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
 210 215 220

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu
 225 230 235 240

Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu
 245 250 255

Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu
 260 265 270

Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
 275 280 285

Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe
 290 295 300

Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu
 305 310 315 320

Gln Gln

(2) INFORMATION FOR SEQ ID NO:150:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:150:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15

Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala

-356-

| | | | | | |
|---|----|-----|----|-----|-----|
| | 20 | | 25 | | 30 |
| Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu | 35 | | 40 | | 45 |
| Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser | 50 | | 55 | | 60 |
| Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu | 65 | | 70 | | 75 |
| His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly | | 85 | | 90 | 95 |
| Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val | | 100 | | 105 | 110 |
| Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met | | 115 | | 120 | 125 |
| Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser | | 130 | | 135 | 140 |
| Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln | | 145 | | 150 | 155 |
| Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro | | 165 | | 170 | 175 |
| Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile | | 180 | | 185 | 190 |
| Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro | | 195 | | 200 | 205 |
| Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu | | 210 | | 215 | 220 |
| Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu | | 225 | | 230 | 235 |
| Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu | | 245 | | 250 | 255 |
| Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu | | 260 | | 265 | 270 |
| Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala | | 275 | | 280 | 285 |
| Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe | | 290 | | 295 | 300 |
| Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu | | 305 | | 310 | 315 |
| Gln Gln | | | | | 320 |

-357-

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 349 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:151:

```

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
1      5      10      15
Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
20      25      30
Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
35      40      45
Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
50      55      60
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
65      70      75      80
His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
85      90      95
Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
100     105     110
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
115     120     125
Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
130     135     140
Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
145     150     155     160
Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165     170     175
Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val Asn Ala Gly
180     185     190
Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Gly Gly Gly Ser
195     200     205
Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Gly
210     215     220
Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn Met Ala Asn Cys
225     230     235     240
Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn
245     250     255

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-358-

Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
 260 265 270

Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
 275 280 285

Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
 290 295 300

Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
 305 310 315 320

Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
 325 330 335

Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 340 345

(2) INFORMATION FOR SEQ ID NO:152:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30

Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly
 115 120 125

Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 130 135 140

Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp

-359-

145 150 155 160
 Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
 165 170 175
 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
 180 185 190
 Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
 195 200 205
 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
 210 215 220
 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
 225 230 235 240
 Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
 245 250 255
 Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
 260 265 270
 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
 275 280 285
 His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
 290 295 300
 Ala Gln Pro
 305

(2) INFORMATION FOR SEQ ID NO:153:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 244 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30
 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

-360-

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
 130 135 140
 His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
 145 150 155 160
 Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn
 165 170 175
 Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly
 180 185 190
 Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
 195 200 205
 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
 210 215 220
 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala
 225 230 235 240
 Gln Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:154:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:154:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30
 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro

-361-

| | | | | | | |
|---|-----|----|-----|----|-----|-----|
| 65 | | 70 | | 75 | | 80 |
| Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg | 85 | | 90 | | 95 | |
| Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln | 100 | | 105 | | 110 | |
| Gln Tyr Val Ile Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro | 115 | | 120 | | 125 | |
| Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser | 130 | | 135 | | 140 | |
| Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser | 145 | | 150 | | 155 | 160 |
| Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly | 165 | | 170 | | 175 | |
| Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro | 180 | | 185 | | 190 | |
| Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro | 195 | | 200 | | 205 | |
| Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser | 210 | | 215 | | 220 | |
| Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu | 225 | | 230 | | 235 | 240 |
| Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu | 245 | | 250 | | 255 | |
| Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu | 260 | | 265 | | 270 | |
| Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe | 275 | | 280 | | 285 | |
| Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His | 290 | | 295 | | 300 | |
| Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala | 305 | | 310 | | 315 | 320 |
| Gln Pro | | | | | | |

(2) INFORMATION FOR SEQ ID NO:155:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

-362-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:155:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30
 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45
 Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 145 150 155 160
 Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
 165 170 175
 Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu
 180 185 190
 Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
 195 200 205
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 210 215 220
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 225 230 235 240
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 245 250 255
 Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:156:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

-363-

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:156:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15
 Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30
 Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
 35 40 45
 Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60
 Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu
 65 70 75 80
 His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95
 Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110
 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125
 Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140
 Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160
 Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
 180 185 190
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
 195 200 205
 Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
 210 215 220
 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu
 225 230 235 240
 Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu
 245 250 255
 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu
 260 265 270
 Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
 275 280 285

-364-

Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe
 290 295 300

Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu
 305 310 315 320

Gln Gln

(2) INFORMATION FOR SEQ ID NO:157:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:157:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15

Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
 35 40 45

Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60

Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu
 65 70 75 80

His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95

Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
 180 185 190

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro

-365-

| | | |
|---|-----|-------------|
| 195 | 200 | 205 |
| Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu | | |
| 210 | 215 | 220 |
| Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu | | |
| 225 | 230 | 235 240 |
| Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu | | |
| | 245 | 250 255 |
| Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu | | |
| | 260 | 265 270 |
| Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala | | |
| | 275 | 280 285 |
| Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe | | |
| | 290 | 295 300 |
| Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu | | |
| | 305 | 310 315 320 |
| Gln Gln | | |

(2) INFORMATION FOR SEQ ID NO:158:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:158:

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Thr | Pro | Leu | Gly | Pro | Ala | Ser | Ser | Leu | Pro | Gln | Ser | Phe | Leu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Leu | Lys | Cys | Leu | Glu | Gln | Val | Arg | Lys | Ile | Gln | Gly | Asp | Gly | Ala | Ala |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Leu | Gln | Glu | Lys | Leu | Cys | Ala | Thr | Tyr | Lys | Leu | Cys | His | Pro | Glu | Glu |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Leu | Val | Leu | Leu | Gly | His | Ser | Leu | Gly | Ile | Pro | Trp | Ala | Pro | Leu | Ser |
| | 50 | | | | | 55 | | | | 60 | | | | | |
| Ser | Cys | Pro | Ser | Gln | Ala | Leu | Gln | Leu | Ala | Gly | Cys | Leu | Ser | Gly | Leu |
| 65 | | | | 70 | | | | | 75 | | | | | 80 | |
| His | Ser | Gly | Leu | Phe | Leu | Tyr | Gln | Gly | Leu | Leu | Gln | Ala | Leu | Glu | Gly |
| | | | 85 | | | | | 90 | | | | | | 95 | |
| Ile | Ser | Pro | Glu | Leu | Gly | Pro | Thr | Leu | Asp | Thr | Leu | Gln | Leu | Asp | Val |
| | | | 100 | | | | | 105 | | | | | | 110 | |

-366-

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly
 180 185 190

Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 195 200 205

Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
 210 215 220

Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu
 225 230 235 240

Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
 245 250 255

Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 260 265 270

Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 275 280 285

Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 290 295 300

Glu Gln Gln
 305

(2) INFORMATION FOR SEQ ID NO:159:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:159:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15

Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu

-367-

| | | |
|---|-----|-----|
| 35 | 40 | 45 |
| Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser | | |
| 50 | 55 | 60 |
| Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu | | |
| 65 | 70 | 75 |
| His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly | | |
| | 85 | 90 |
| Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val | | |
| | 100 | 105 |
| Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met | | |
| | 115 | 120 |
| Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser | | |
| | 130 | 135 |
| Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln | | |
| | 145 | 150 |
| Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro | | |
| | 165 | 170 |
| Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly | | |
| | 180 | 185 |
| Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His | | |
| | 195 | 200 |
| Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp | | |
| | 210 | 215 |
| Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu | | |
| | 225 | 230 |
| Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile | | |
| | 245 | 250 |
| Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala | | |
| | 260 | 265 |
| Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu | | |
| | 275 | 280 |
| Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln | | |
| | 290 | 295 |
| Glu Gln Gln | | |
| 305 | | |

(2) INFORMATION FOR SEQ ID NO:160:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 128 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

-368-

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:

```

Met Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His
1           5           10           15
Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp
20           25           30
Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe
35           40           45
Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys
50           55           60
Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met
65           70           75           80
Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser
85           90           95
Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys
100          105          110
Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu
115          120          125

```

(2) INFORMATION FOR SEQ ID NO:161:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 176 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:161:

```

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
1           5           10           15
Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
20           25           30
Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
35           40           45
Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
50           55           60
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
65           70           75           80

```

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| His | Ser | Gly | Leu | Phe | Leu | Tyr | Gln | Gly | Leu | Gln | Ala | Leu | Gly | | |
| | | | | 85 | | | | | 90 | | | | 95 | | |
| Ile | Ser | Pro | Glu | Leu | Gly | Pro | Thr | Leu | Asp | Thr | Leu | Gln | Leu | Asp | Val |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Ala | Asp | Phe | Ala | Thr | Thr | Ile | Trp | Gln | Gln | Met | Glu | Glu | Leu | Gly | Met |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Ala | Pro | Ala | Leu | Gln | Pro | Thr | Gln | Gly | Ala | Met | Pro | Ala | Phe | Ala | Ser |
| | | 130 | | | | 135 | | | | | 140 | | | | |
| Ala | Phe | Gln | Arg | Arg | Ala | Gly | Gly | Val | Leu | Val | Ala | Ser | His | Leu | Gln |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Ser | Phe | Leu | Glu | Val | Ser | Tyr | Arg | Val | Leu | Arg | His | Leu | Ala | Gln | Pro |
| | | | | 165 | | | | | 170 | | | | | 175 | |

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 176 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:162:

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Thr | Pro | Leu | Gly | Pro | Ala | Ser | Ser | Leu | Pro | Gln | Ser | Phe | Leu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Leu | Lys | Ser | Leu | Glu | Gln | Val | Arg | Lys | Ile | Gln | Gly | Asp | Gly | Ala | Ala |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Leu | Gln | Glu | Lys | Leu | Cys | Ala | Thr | Tyr | Lys | Leu | Cys | His | Pro | Glu | Glu |
| | | | 35 | | | | 40 | | | | | 45 | | | |
| Leu | Val | Leu | Leu | Gly | His | Ser | Leu | Gly | Ile | Pro | Trp | Ala | Pro | Leu | Ser |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Ser | Cys | Pro | Ser | Gln | Ala | Leu | Gln | Leu | Ala | Gly | Cys | Leu | Ser | Gln | Leu |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| His | Ser | Gly | Leu | Phe | Leu | Tyr | Gln | Gly | Leu | Leu | Gln | Ala | Leu | Glu | Gly |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Ile | Ser | Pro | Glu | Leu | Gly | Pro | Thr | Leu | Asp | Thr | Leu | Gln | Leu | Asp | Val |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Ala | Asp | Phe | Ala | Thr | Thr | Ile | Trp | Gln | Gln | Met | Glu | Glu | Leu | Gly | Met |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Ala | Pro | Ala | Leu | Gln | Pro | Thr | Gln | Gly | Ala | Met | Pro | Ala | Phe | Ala | Ser |
| | 130 | | | | | 135 | | | | | | 140 | | | |

-370-

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:163:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 186 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:163:

Met Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala Ala Pro
 1 5 10 15
 His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg
 20 25 30
 Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys
 35 40 45
 Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu
 50 55 60
 Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe
 65 70 75 80
 Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu Leu Glu Phe
 85 90 95
 Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu
 100 105 110
 Gln Ala Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile Gln Phe Leu
 115 120 125
 Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr
 130 135 140
 Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu
 145 150 155 160
 Gln Asp Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu
 165 170 175
 Gln Ser Ser Leu Arg Ala Leu Arg Gln Met
 180 185

(2) INFORMATION FOR SEQ ID NO:164:

(i) SEQUENCE CHARACTERISTICS:

-371-

- (A) LENGTH: 155 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:164:

```

Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys
1           5           10           15
Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
20           25           30
Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe
35           40           45
Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp
50           55           60
Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala Arg
65           70           75           80
Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser
85           90           95
Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
100          105          110
Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala
115          120          125
Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu
130          135          140
Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg
145          150          155

```

(2) INFORMATION FOR SEQ ID NO:165:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 286 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:

```

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1           5           10           15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp

```

20

25

30

(2) INFORMATION FOR SEQ ID NO:166:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 286 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

-373-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly
 115 120 125

Gly Ser Asn Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val
 130 135 140

Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser
 145 150 155 160

Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala
 165 170 175

Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys
 180 185 190

Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met
 195 200 205

Ala Ala Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly
 210 215 220

Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu
 225 230 235 240

Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp
 245 250 255

Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val
 260 265 270

Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg
 275 280 285

(2) INFORMATION FOR SEQ ID NO:167:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 286 amino acids

-374-

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:

```

Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys
1           5           10           15
Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
20          25          30
Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe
35          40          45
Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp
50          55          60
Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala Arg
65          70          75          80
Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser
85          90          95
Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
100         105         110
Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala
115         120         125
Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu
130         135         140
Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg Tyr Val Ile Glu Gly
145         150         155         160
Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala Asn
165         170         175
Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro
180         185         190
Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile
195         200         205
Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
210         215         220
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg
225         230         235         240
Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His
245         250         255
Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
260         265         270

```


-375-

Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 275 280 285

(2) INFORMATION FOR SEQ ID NO:168:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 290 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:

Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys
 1 5 10 15

Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
 20 25 30

Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe
 35 40 45

Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp
 50 55 60

Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala Arg
 65 70 75 80

Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser
 85 90 95

Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
 100 105 110

Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala
 115 120 125

Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu
 130 135 140

Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg Glu Phe His Ala Tyr
 145 150 155 160

Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser
 165 170 175

Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
 180 185 190

Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu
 195 200 205

Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu
 210 215 220

Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu

-376-

225 230 235 240
 Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
 245 250 255
 Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe
 260 265 270
 Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu
 275 280 285
 Gln Gln
 290

(2) INFORMATION FOR SEQ ID NO:169:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 45 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:169:

ACGTCCATGG CNTCNCNGC NCCNCCTGCT TGTGACCTCC GAGTC

45

(2) INFORMATION FOR SEQ ID NO:170:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 34 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:170:

AATAGCTGAA TTCTTACCCT TCCTGAGACA GATT

34

(2) INFORMATION FOR SEQ ID NO:171:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 33 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

-377-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:171:

TGACAAGCTT ACCTGACGCA GAGGGTGGAC CCT

33

(2) INFORMATION FOR SEQ ID NO:172:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:172:

ATGCACGAAT TCCCTGACGC AGAGGGTGGGA

30

(2) INFORMATION FOR SEQ ID NO:173:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 14 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:173:

AATTCATGC ATAC

14

(2) INFORMATION FOR SEQ ID NO:174:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:174:

GGTACGTATG

10

(2) INFORMATION FOR SEQ ID NO:175:

-378-

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 561 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:175:

| | |
|--|-----|
| ATGGCTCCAG TACCACCAGG TGAAGATTCC AAAGATGTGG CCGCCCCACA CAGACAGCCA | 60 |
| CTCACCTCTT CAGAACGAAT TGACAAACAA ATTCTGGTACA TCCTCGACGG GATATCAGCC | 120 |
| CTGAGAAAGG AGACATGTAA CAAGAGTAAC ATGTGTGAAA GCAGCAAAGA GCGCTAGCA | 180 |
| GAAAACAACC TGAACCTTCC AAAGATGGCT GAAAAAGATG GATGCTTCCA ATCCGGATTC | 240 |
| AATGAGGAGA CTTGCCTGGT GAAAATCATC ACTGGTCTTT TGGAGTTGA GGTATACCTC | 300 |
| GAGTACCTCC AGAACAGATT TGAGAGTAGT GAGGAACAAG CCAGAGCTGT GCAGATGTCG | 360 |
| ACAAAAGTCC TGATCCAGTT CCTGCAGAAA AAGGCAAAGA ATCTAGATGC AATAACCACC | 420 |
| CCTGACCCAA CCACAAATGC ATCCCTGCTG ACGAAGCTGC AGGCACAGAA CCAGTGGCTG | 480 |
| CAGGACATGA CAACTCATCT CATTCTGCGC AGCTTTAAGG AGTTCCTGCA GTCCAGCCTG | 540 |
| AGGGCTCTTC GGCAAATGTA G | 561 |

(2) INFORMATION FOR SEQ ID NO:176:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 402 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:

| | |
|---|-----|
| ATGGCACCGG CTCGTTCCCC GTCCCCGTCT ACCCAGCCGT GGGAACACGT GAATGCCATC | 60 |
| CAGGAGGCCC GCGCTCTCCT GAACCTGAGT AGAGACACTG CTGCTGAGAT GAATGAAACA | 120 |
| GTAGAAGTGA TATCAGAAAT GTTTGACCTC CAGGAGCCGA CTTGCCTACA GACCCGCCTG | 180 |
| GAGCTGTACA AGCAGGGCCT GCGGGGCAGC CTCACCAAGC TCAAGGGCCC CTTGACCATG | 240 |
| ATGGCCAGCC ACTACAAGCA GCACTGCCCT CCAACCCCGG AACTTCCTG TGCAACCCAG | 300 |
| ATTATCACCT TTGAAAGTTT CAAAGAGAAC CTGAAGGACT TCCTGCTTGT CATCCCCTTT | 360 |
| GACTGCTGGG AGCCAGTCCA GGAGTGATAA GGATCCGAAT TC | 402 |

-379-

(2) INFORMATION FOR SEQ ID NO:177:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 546 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:177:

| | |
|---|-----|
| ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTG ATAAGGATCC | 540 |
| GAATTC | 546 |

(2) INFORMATION FOR SEQ ID NO:178:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 546 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:

| | |
|---|-----|
| ATGGCTACAC CATTAGGACC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG | 360 |

-380-

| | |
|---|-----|
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTG ATAAGGATCC | 540 |
| GAATTC | 546 |

(2) INFORMATION FOR SEQ ID NO:179:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 546 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:179:

| | |
|--|-----|
| ATGGCTACAC CATTGGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTCTTTA | 60 |
| GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC | 120 |
| TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG | 180 |
| GCTCCCCCTGA GCTCCTGCCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC | 240 |
| CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCCC TGGAAGGGAT ATCCCCGAG | 300 |
| TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCGG ACTTTGCCAC CACCATCTGG | 360 |
| CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG | 420 |
| GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG | 480 |
| AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTG ATAAGGATCC | 540 |
| GAATTC | 546 |

(2) INFORMATION FOR SEQ ID NO:180:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 465 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:180:

| | |
|---|-----|
| ATGGCGTCTC CGGCGCCGCC TGCTTGTGAC CTCCGAGTCC TCAGTAAACT GCTTCGTGAC | 60 |
| TCCCATGTCC TTCACAGCAG ACTGAGCCAG TGCCCAGAGG TTCACCCTTT GCCTACACCT | 120 |

-381-

| | |
|--|-----|
| GTCCTGCTGC CTGCTGTGGA CTTTAGCTTG GGAGAATGGA AAACCCAGAT GGAGGAGACC | 180 |
| AAGGCACAGG ACATTCTGGG AGCAGTGACC CTTCTGCTGG AGGGAGTGAT GGCAGCACGG | 240 |
| GGACAACCTGG GACCCACTTG CCTCTCATCC CTCCTGGGGC AGCTTTCTGG ACAGGTCCGT | 300 |
| CTCCTCCTTG GGGCCCTGCA GAGCCTCCTT GGAACCCAGC TTCCTCCACA GGCAGGACC | 360 |
| ACAGCTCACA AGGATCCCAA TGCCATCTTC CTGAGCTTCC AACACCTGCT CCGAGGAAAG | 420 |
| GTGCGTTTCC TGATGCTTGT AGGAGGGTCC ACCCTCTGCG TCAGG | 465 |

(2) INFORMATION FOR SEQ ID NO:181:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 143 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:

| | |
|---|-----|
| CCTGTCAACC CGGGCGGCGG CTCTGGTGGT GGTTCTGGTG GCGGCTCTGA GGGTGGCGGC | 60 |
| TCTGAGGGTG GCGTTCTGA GGGTGGCGGC TCTGAGGGTG GCGGTTCCGG TGGCGGCTCC | 120 |
| GGTTCGGTA ACATGTATTA TGA | 143 |

(2) INFORMATION FOR SEQ ID NO:182:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 180 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:182:

| | |
|---|-----|
| ATCGTCTGAC CTCCCGGGCC TCCTGTCAAT GCTGGCGGCG GCTCTGGTGG TGTTCTGGT | 60 |
| GGCGGCTCTG AGGGTGGCGG CTCTGAGGGT GCGGTTCTG AGGGTGGCGG CTCTGAGGGT | 120 |
| GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT GATTTTGATT ATGAAAACAT GTCAAACGCT | 180 |

(2) INFORMATION FOR SEQ ID NO:183:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 858 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

-382-

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:183:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGAAGGATT | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCGT CTCCGGCGCC GCCTGCTTGT | 420 |
| GACCTCCGAG TCCTCAGTAA ACTGCTTCGT GACTCCCATG TCCTTCACAG CAGACTGAGC | 480 |
| CAGTGCCAG AGGTTACCC TTTGCCTACA CCTGTCTGCTG TGCCTGCTGT GGACTTTAGC | 540 |
| TTGGGAGAAT GGAAAACCCA GATGGAGGAG ACCAAGGCAC AGGACATTCT GGGAGCAGTG | 600 |
| ACCCTTCTGC TGGAGGGAGT GATGGCAGCA CGGGGACAAC TGGGACCCAC TTGCCTCTCA | 660 |
| TCCCTCCTGG GGCAGCTTTC TGGACAGGTC CGTCTCCTCC TTGGGGCCCT GCAGAGCCTC | 720 |
| CTTGAACCC AGCTTCTCTC ACAGGGCAGG ACCACAGCTC ACAAGGATCC CAATGCCATC | 780 |
| TTCTGAGCT TCCAACACCT GCTCCGAGGA AAGGTGCGTT TCCTGATGCT TGTAGGAGGG | 840 |
| TCCACCCTCT GCGTCAGG | 858 |

(2) INFORMATION FOR SEQ ID NO:184:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 858 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:184:

| | |
|---|-----|
| ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC | 60 |
| CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC | 120 |
| CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA | 180 |
| GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC | 240 |

-383-

| | |
|---|-----|
| TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCGGGA AAAACTGACG | 300 |
| TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC | 360 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCGT CTCCGGCGCC GCCTGCTTGT | 420 |
| GACCTCCGAG TCCTCAGTAA ACTGCTTCGT GACTCCCATG TCCTTCACAG CAGACTGAGC | 480 |
| CAGTGCCAG AGGTTACCCC TTTGCCTACA CCTGTCTGCG TGCCTGCTGT GGACTTTAGC | 540 |
| TTGGGAGAAT GGAAAACCCA GATGGAGGAG ACCAAGGCAC AGGACATTCT GGGAGCAGTG | 600 |
| ACCCTTCTGC TGGAGGGAGT GATGGCAGCA CGGGGACAAC TGGGACCCAC TTGCCTCTCA | 660 |
| TCCCTCCTGG GGCAGCTTTC TGGACAGGTC CGTCTCCTCC TTGGGGCCCT GCAGAGCCTC | 720 |
| CTTGAACCC AGCTTCCTCC ACAGGGCAGG ACCACAGCTC ACAAGGATCC CAATGCCATC | 780 |
| TTCCTGAGCT TCCAACACCT GCTCCGAGGA AAGGTGCGTT TCCTGATGCT TGTAGGAGGG | 840 |
| TCCACCCTCT GCGTCAGG | 858 |

(2) INFORMATION FOR SEQ ID NO:185:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 852 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:185:

| | |
|---|-----|
| ATGGCGTCTC CGGCGCCGCC TGCTGTGAC CTCCGAGTCC TCAGTAAACT GCTTCGTGAC | 60 |
| TCCCATGTCC TTCACAGCAG ACTGAGCCAG TGCCAGAGG TTCACCCTTT GCCTACACCT | 120 |
| GTCTGTCTGC CTGCTGTGGA CTTTAGCTTG GGAGAATGGA AAACCCAGAT GGAGGAGACC | 180 |
| AAGGCACAGG ACATTCTGGG AGCAGTGACC CTTCTGCTGG AGGGAGTGAT GGCAGCACGG | 240 |
| GGACAACTGG GACCCACTTG CCTCTCATCC CTCCTGGGGC AGCTTTCTGG ACAGGTCCGT | 300 |
| CTCCTCCTTG GGGCCCTGCA GAGCCTCCTT GGAACCCAGC TTCCTCCACA GGGCAGGACC | 360 |
| ACAGCTCACA AGGATCCCAA TGCCATCTTC CTGAGCTTCC AACACCTGCT CCGAGGAAAG | 420 |
| GTGCGTTTCC TGATGCTTGT AGGAGGGTCC ACCCTCTGCG TCAGGATCGA GGAAGGATT | 480 |
| TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT | 540 |
| GAAATTATAC ATCACTTAAA GAGACCACCT AACCCTTTGC TGGACCCGAA CAACCTCAAT | 600 |
| TCTGAAGACA TGGATATCCT GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTC | 660 |
| GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC | 720 |

-384-

CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA 780
GGTGACTGGC AAGAATCCG GGAAAACTG ACGTTCTATC TGGTTACCCT TGAGCAAGCG 840
CAGGAACAAC AG 852

(2) INFORMATION FOR SEQ ID NO:186:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 870 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:186:

ATGGCGTCTC CGGCGCCGCC TGCTTGTGAC CTCCGAGTCC TCAGTAACT GCTTCGTGAC 60
TCCCATGTCC TTCACAGCAG ACTGAGCCAG TGCCAGAGG TTCACCCTTT GCCTACACCT 120
GTCCTGCTGC CTGCTGTGGA CTTTAGCTTG GGAGAATGGA AAACCCAGAT GGAGGAGACC 180
AAGGCACAGG ACATTCTGGG AGCAGTGACC CTTCTGCTGG AGGGAGTGAT GGCAGCACGG 240
GGACAACTGG GACCCACTTG CCTCTCATCC CTCCTGGGGC AGCTTTCTGG ACAGGTCCGT 300
CTCCTCCTTG GGGCCCTGCA GAGCCTCCTT GGAACCCAGC TTCCTCCACA GGGCAGGACC 360
ACAGCTCACA AGGATCCCAA TGCCATCTTC CTGAGCTTCC AACACCTGCT CCGAGGAAAG 420
GTGCGTTTCC TGATGCTTGT AGGAGGGTCC ACCCTCTGCG TCAGGGAATT CCATGCATAC 480
GTAGAGGGCG GTGGAGGCTC CCCGGGTGGT GGTTCCTGGCG GCGGCTCCAA CATGGCTAAC 540
TGCTCTATAA TGATCGATGA AATTATACAT CACTTAAAGA GACCACCTAA CCCTTTGCTG 600
GACCCGAACA ACCTCAATTC TGAAGACATG GATATCCTGA TGGAAACGAA CCTTCGAAC 660
CCAAACCTGC TCGCATTCGT AAGGGCTGTC AAGCACTTAG AAAATGCATC AGGTATTGAG 720
GCAATCTTTC GTAATCTCCA ACCATGTCTG CCCTCTGCCA CGGCCGCACC CTCTCGACAT 780
CCAATCATCA TCAAGGCAGG TGAATGGCAA GAATTCGGG AAAAAGTAC GTTCTATCTG 840
GTTACCCTTG AGCAAGCGCA GGAACAACAG 870

(2) INFORMATION FOR SEQ ID NO:187:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

-385-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:187:

Met Ser Arg Leu Pro Val Leu Leu Leu Leu Gln Leu Leu Val Arg Pro
1 5 10 15

Ala Met

(2) INFORMATION FOR SEQ ID NO:188:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:188:

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Asn

(2) INFORMATION FOR SEQ ID NO:189:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:189:

Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Asn

(2) INFORMATION FOR SEQ ID NO:190:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

-386-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:190:

Tyr Val Glu Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Asn

(2) INFORMATION FOR SEQ ID NO:191:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 33 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:191:

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile
1 5 10 15

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
20 25 30

Asn

(2) INFORMATION FOR SEQ ID NO:192:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 33 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:192:

Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile
1 5 10 15

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
20 25 30

Asn

(2) INFORMATION FOR SEQ ID NO:193:

-387-

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 33 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:193:

Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
1 5 10 15
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
 20 25 30

Asn

(2) INFORMATION FOR SEQ ID NO:194:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 49 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:194:

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly
1 5 10 15
Ser Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu
 20 25 30
Gly Gly Gly Ser Glu Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Gly
 35 40 45

Asn

(2) INFORMATION FOR SEQ ID NO:195:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 60 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

-388-

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:195:

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val Asn Ala Gly
 1 5 10 15
 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Gly Gly Gly Ser
 20 25 30
 Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Gly
 35 40 45
 Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn
 50 55 60

(2) INFORMATION FOR SEQ ID NO:196:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:196:

Glu Phe His Ala Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly
 1 5 10 15
 Ser Gly Gly Gly Ser Asn
 20

389

WHAT IS CLAIMED IS:

1. A fusion protein having the formula selected from the group consisting of

5

R₁-L-R₂, R₂-L-R₁, R₁-R₂, R₂-R₁, R₁-L-R₁ and R₁-R₁
 wherein R₁ is a human interleukin-3 mutant
 polypeptide of the Formula:

10 Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
 1 5 10 15

Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 20 25 30

15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa Xaa
 35 40 45

20

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 50 55 60

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 65 70 75

25

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 80 85 90

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 95 100 105

30

Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 110 115 120

Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe

390

125

130

[SEQ ID NO:1]

wherein

- 5 Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or Arg;
- Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
- Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
- 10 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
- Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, Asn, Thr, Ser or Val;
- 15 Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, Gln, Leu, Val or Gly;
- Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys, Phe, Leu, Ser, or Arg;
- Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu;
- 20 Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala;
- Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp;
- 25 Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
- Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or Trp;
- Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;
- Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, or Lys;
- 30 Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln;
- Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or Glu;

391

Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;

Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln,

Thr, Arg, Ala, Phe, Ile or Met;

Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or

5 Val;

Xaa at position 36 is Asp, Leu, or Val;

Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile;

Xaa at position 38 is Asn, or Ala;

Xaa at position 40 is Leu, Trp, or Arg;

10 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or
Pro;

Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr,
Leu, Val, Glu, Phe, Tyr, Ile, Met or Ala;

15 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
Cys, Gln, Arg, Thr, Gly or Ser;

Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met,
Trp, Glu, Asn, Gln, Ala or Pro;

Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr,
Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His;

20 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,
Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;

Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or
His;

25 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe,
Glu, Lys, Thr, Ala, Met, Val or Asn;

Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
or Asp;

Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn,
Ser, Ala, Ile, Val, His, Phe, Met or Gln;

30 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
His;

Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or
Thr;

Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys,

- Ser, or Met;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala or Leu;
- Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- 5 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
- Xaa at position 57 is Asn or Gly;
- Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;
- 10 Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;
- Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr;
- Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
- Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, Asp, or
- 15 Ile;
- Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val;
- Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;
- Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or
- 20 Ser;
- Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;
- Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His;
- 25 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;
- Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or Leu;
- Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 30 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, Trp, or Asn;
- Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;
- Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr,

- or Arg;
- Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu;
- 5 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;
- Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;
- Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- 10 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or Asp;
- Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or Arg;
- Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or Lys;
- 15 Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
- Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;
- Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
- 20 Xaa at position 85 is Leu, Asn, Val, or Gln;
- Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
- Xaa at position 87 is Leu, Ser, Trp, or Gly;
- Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
- Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, or Ser;
- 25 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or Met;
- Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or His;
- 30 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, Ile or Leu;
- Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;
- Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln,

- Lys, His, Ala, or Pro;
- Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly,
Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;
- Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- 5 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;
- Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
Gly, Ser, Phe, or His;
- 10 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
Gln, or Pro;
- Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;
- Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or
15 Pro;
- Xaa at position 103 is Asp, or Ser;
- Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
Leu, Gln, Lys, Ala, Phe, or Gly;
- Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
20 Tyr, Leu, Lys, Ile, Asp, or His;
- Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
or Pro;
- Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln,
His, Ser, Ala or Pro;
- 25 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,
or Gly;
- Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln,
His, Glu, Ser, Ala, or Trp;
- Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;
- 30 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser,
or Phe;
- Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr,
Asp, Lys, Leu, Ile, Val or Asn;
- Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or

395

Leu;

Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His,
Thr, Trp, or Met;

5 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val,
Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or
Ile;

Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or
Pro;

10 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp,
or Tyr;

Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr,
or Arg;

Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or
Gln;

15 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp,
or Gly;

Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;

20 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr,
or Leu;

and which can additionally have Met- preceding the amino acid in
position 1; and wherein from 1 to 14 amino acids can be deleted
from the N-terminus and/or from 1 to 15 amino acids can be deleted
25 from the C-terminus; and wherein from 4 to 44 of the amino acids
designated by Xaa are different from the corresponding amino acids
of native (1-133) human interleukin-3;

30 R₂ is a Il-3, Il-3 variant or a colony stimulating factor;
and

L is a linker capable of Linking R₁ to R₂.

2. The fusion protein of claim 1 wherein said colony

stimulating factor is selected from the group consisting of GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, 5 human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF)

397

3. The fusion protein of claim 2 wherein R₁ is of the Formula:

| | | | | | | | |
|----|---|---|-----|--|-----|--|-----|
| 5 | 1 | | 5 | | 10 | | 15 |
| | | Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn | | | | | |
| | | Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Xaa Leu Lys Xaa Xaa | 20 | | 25 | | 30 |
| 10 | | Xaa Xaa Xaa Xaa Xaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa Xaa | 35 | | 40 | | 45 |
| | | Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu Xaa | 50 | | 55 | | 60 |
| 15 | | Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile Glu | 65 | | 70 | | 75 |
| | | Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr Ala | 80 | | 85 | | 90 |
| 20 | | Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa Xaa | 95 | | 100 | | 105 |
| | | Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Xaa Leu Glu Xaa | 110 | | 115 | | 120 |
| | | Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe | 125 | | 130 | | |
| 30 | | [SEQ ID NO:2] | | | | | |

wherein

Xaa at position 17 is Ser, Gly, Asp, Met, or Gln;

Xaa at position 18 is Asn, His, or Ile;

- Xaa at position 19 is Met or Ile;
Xaa at position 21 is Asp or Glu;
Xaa at position 23 is Ile, Ala, Leu, or Gly;
Xaa at position 24 is Ile, Val, or Leu;
5 Xaa at position 25 is Thr, His, Gln, or Ala;
Xaa at position 26 is His or Ala;
Xaa at position 29 is Gln, Asn, or Val;
Xaa at position 30 is Pro, Gly, or Gln;
Xaa at position 31 is Pro, Asp, Gly, or Gln;
10 Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or
Glu;
Xaa at position 33 is Pro or Glu;
Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Ala, Arg,
Gln, Glu, Ile, Phe, Thr or Met;
15 Xaa at position 35 is Leu, Ala, Asn, Pro, Gln, or Val;
Xaa at position 37 is Phe, Ser, Pro, or Trp;
Xaa at position 38 is Asn or Ala;
Xaa at position 42 is Gly, Asp, Ser, Cys, Ala, Asn, Ile,
Leu, Met, Tyr or Arg;
20 Xaa at position 44 is Asp or Glu;
Xaa at position 45 is Gln, Val, Met, Leu, Thr, Ala, Asn,
Glu, Ser or Lys;
Xaa at position 46 is Asp, Phe, Ser, Thr, Ala, Asn Gln,
Glu, His, Ile, Lys, Tyr, Val or Cys;
25 Xaa at position 50 is Glu, Ala, Asn, Ser or Asp;
Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
His;
Xaa at position 54 is Arg or Ala;
Xaa at position 55 is Arg, Thr, Val, Leu, or Gly;
30 Xaa at position 56 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
Glu, Leu, Thr, Val or Lys;
Xaa at position 60 is Ala or Ser;
Xaa at position 62 is Asn, Pro, Thr, or Ile;
Xaa at position 63 is Arg or Lys;

- Xaa at position 64 is Ala or Asn;
Xaa at position 65 is Val or Thr;
Xaa at position 66 is Lys or Arg;
Xaa at position 67 is Ser, Phe, or His;
5. Xaa at position 68 is Leu, Ile, Phe, or His;
Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, or Gly;
Xaa at position 71 is Ala, Pro, or Arg;
Xaa at position 72 is Ser, Glu, Arg, or Asp;
10 Xaa at position 73 is Ala or Leu;
Xaa at position 76 is Ser, Val, Ala, Asn, Glu, Pro, or Gly;
Xaa at position 77 is Ile or Leu;
Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
15 Gly, or Asp;
Xaa at position 80 is Asn, Gly, Glu, or Arg;
Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Ala, Asn, Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
Xaa at position 83 is Pro or Thr;
20 Xaa at position 85 is Leu or Val;
Xaa at position 87 is Leu or Ser;
Xaa at position 88 is Ala or Trp;
Xaa at position 91 is Ala or Pro;
Xaa at position 93 is Thr, Asp, Ser, Pro, Ala, Leu, or
25 Arg;
Xaa at position 95 is His, Pro, Arg, Val, Leu, Gly, Asn, Phe, Ser or Thr;
Xaa at position 96 is Pro or Tyr;
Xaa at position 97 is Ile or Val;
30 Xaa at position 98 is His, Ile, Asn, Leu, Ala, Thr, Leu, Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;
Xaa at position 99 is Ile, Leu, or Val;
Xaa at position 100 is Lys, Arg, Ile, Gln, Pro, or Ser;
Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Pro,

400

- Asn, Ile, Leu or Tyr;
 Xaa at position 104 is Trp or Leu;
 Xaa at position 105 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr,
 Leu, Lys, Ile, Asp, or His;
 5 Xaa at position 106 is Glu or Gly;
 Xaa at position 108 is Arg, Ala, or Ser;
 Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;
 Xaa at position 112 is Thr, Val, or Gln;
 Xaa at position 114 is Tyr or Trp;
 10 Xaa at position 115 is Leu or Ala;
 Xaa at position 116 is Lys, Thr, Val, Trp, Ser, Ala, His,
 Met, Phe, Tyr or Ile;
 Xaa at position 117 is Thr or Ser;
 Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
 15 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Asp, or
 Gly;
 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
 His, Ile, Tyr, or Cys;
 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr,
 20 or Leu;

- and which can additionally have Met- preceding the amino
 acid in position 1; and wherein from 1 to 14 amino acids can
 be deleted from the N-terminus and/or from 1 to 15 amino
 25 acids can be deleted from the C-terminus; and wherein from 4
 to 35 of the amino acids designated by Xaa are different
 from the corresponding amino acids of native (1-133)human
 interleukin-3.

- 30 4. The fusion protein of claim 3 wherein R₁ is
 of the Formula:

Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
 1 5 10 15

401

Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa Xaa
 20 25 30
 5 Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa
 35 40 45
 Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala
 50 55 60
 10 Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu
 65 70 75
 Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala
 15 80 85 90
 Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Xaa Gly Asp Trp Xaa
 95 100 105
 20 Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu Xaa
 110 115 120
 Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
 125 130
 25 [SEQ ID NO:3]

wherein

Xaa at position 17 is Ser, Gly, Asp, or Gln;

Xaa at position 18 is Asn, His, or Ile;

30 Xaa at position 23 is Ile, Ala, Leu, or Gly;

Xaa at position 25 is Thr, His, or Gln;

Xaa at position 26 is His or Ala;

Xaa at position 29 is Gln or Asn;

Xaa at position 30 is Pro or Gly;

402

- Xaa at position 32 is Leu, Arg, Asn, or Ala;
Xaa at position 34 is Leu, Val, Ser, Ala, Arg, Gln, Glu,
Ile, Phe, Thr, or Met;
Xaa at position 35 is Leu, Ala, Asn, or Pro;
- 5 Xaa at position 38 is Asn or Ala;
Xaa at position 42 is Gly, Asp, Ser, Ala, Asn, Ile, Leu,
Met, Tyr or Arg;
Xaa at position 45 is Gln, Val, Met, Leu, Ala, Asn, Glu,
or Lys;
- 10 Xaa at position 46 is Asp, Phe, Ser, Gln, Glu, His, Val
or Thr;
Xaa at position 50 is Glu Asn, Ser or Asp;
Xaa at position 51 is Asn, Arg, Pro, Thr, or His;
Xaa at position 55 is Arg, Leu, or Gly;
- 15 Xaa at position 56 is Pro, Gly, Ser, Ala, Asn, Val, Leu or
Gln;
Xaa at position 62 is Asn, Pro, or Thr;
Xaa at position 64 is Ala or Asn;
Xaa at position 65 is Val or Thr;
- 20 Xaa at position 67 is Ser or Phe;
Xaa at position 68 is Leu or Phe;
Xaa at position 69 is Gln, Ala, Glu, or Arg;
Xaa at position 76 is Ser, Val, Asn, Pro, or Gly;
Xaa at position 77 is Ile or Leu;
- 25 Xaa at position 79 is Lys, Gly, Asn, Met, Arg, Ile, or
Gly;
Xaa at position 80 is Asn, Gly, Glu, or Arg;
Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
His, Met, Phe, Ser, Thr, Tyr or Val;
- 30 Xaa at position 87 is Leu or Ser;
Xaa at position 88 is Ala or Trp;
Xaa at position 91 is Ala or Pro;
Xaa at position 93 is Thr, Asp, or Ala;
Xaa at position 95 is His, Pro, Arg, Val, Gly, Asn, Ser or

403

Thr;

Xaa at position 98 is His, Ile, Asn, Ala, Thr, Gln, Glu,
Lys, Met, Ser, Tyr, Val or Leu;

Xaa at position 99 is Ile or Leu;

5 Xaa at position 100 is Lys or Arg;

Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Pro,
Asn, Ile, Leu or Tyr;

Xaa at position 105 is Asn, Pro, Ser, Ile or Asp;

Xaa at position 108 is Arg, Ala, or Ser;

10 Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;

Xaa at position 112 is Thr or Gln;

Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, Tyr
or Ile;

Xaa at position 117 is Thr or Ser;

15 Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;

Xaa at position 121 is Ala, Ser, Ile, Pro, or Asp;

Xaa at position 122 is Gln, Met, Trp, Phe, Pro, His, Ile,
or Tyr;

Xaa at position 123 is Ala, Met, Glu, Ser, or Leu;

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and which can additionally have Met- preceding the amino
acid in position 1; and wherein from 1 to 14 amino acids can
be deleted from the N-terminus and/or from 1 to 15 amino
acids can be deleted from the C-terminus; and wherein from 4
25 to 44 of the amino acids designated by Xaa are different
from the corresponding amino acids of native (1-133)human
interleukin-3.

5. The fusion protein of claim 4 wherein R₁
30 is of the Formula:

Xaa at position 42 is Gly, Asp, Ser, Ile, Leu, Met, Tyr,
or Ala;

35 Xaa at position 45 is Gln, Val, Met or Asn;

Xaa at position 46 is Asp, Ser, Gln, His or Val;

Xaa at position 51 is Asn, Pro or Thr;

5 Xaa at position 76 is Ser, or Pro;

Xaa at position 95 is His, Arg, Thr, Asn or Ser;

10 Ser, Tyr or Val;

Xaa at position 101 is Asp, Pro, His, Asn, Ile or Leu;

Xaa at position 108 is Arg, Ala, or Ser;

Xaa at position 121 is Ala, or Ile;

Xaa at position 123 is Ala, Met or Glu.

6. A fusion protein having the formula selected from the group consisting of

25 wherein R₁ is a human interleukin-3 mutant
polypeptide of the Formula:

1 5 . . 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa

405

| | | | |
|----|---|-----|-----|
| | 35 | 40 | 45 |
| | Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa | | |
| | 50 | 55 | 60 |
| 5 | Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa | | |
| | 65 | 70 | 75 |
| | Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa | | |
| 10 | 80 | 85 | 90 |
| | Xaa Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa | | |
| | 95 | 100 | 105 |
| 15 | Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:4] | | |
| | 110 | | |

wherein

- Xaa at position 3 is Ser, Lys, Gly, Asp, Met, Gln, or Arg;
- 20 Xaa at position 4 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
- Xaa at position 5 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
- Xaa at position 6 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
- Xaa at position 7 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,
Gln, Asn, Thr, Ser or Val;
- 25 Xaa at position 8 is Glu, Trp, Pro, Ser, Ala, His, Asp,
Asn, Gln, Leu, Val, or Gly;
- Xaa at position 9 is Ile, Val, Ala, Leu, Gly, Trp, Lys,
Phe, Leu, Ser, or Arg;
- Xaa at position 10 is Ile, Gly, Val, Arg, Ser, Phe, or
30 Leu;
- Xaa at position 11 is Thr, His, Gly, Gln, Arg, Pro, or
Ala;
- Xaa at position 12 is His, Thr, Phe, Gly, Arg, Ala, or
Trp;

- Xaa at position 13 is Leu, Gly, Arg, Thr, Ser, or Ala;
Xaa at position 14 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
Trp;
Xaa at position 15 is Gln, Asn, Leu, Pro, Arg, or Val;
5 Xaa at position 16 is Pro, His, Thr, Gly, Asp, Gln, Ser,
Leu, or Lys;
Xaa at position 17 is Pro, Asp, Gly, Ala, Arg, Leu, or
Gln;
Xaa at position 18 is Leu, Val, Arg, Gln, Asn, Gly, Ala,
10 or Glu;
Xaa at position 19 is Pro, Leu, Gln, Ala, Thr, or Glu;
Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
Thr, Arg, Ala, Phe, Ile or Met;
Xaa at position 21 is Leu, Ala, Gly, Asn, Pro, Gln, or
15 Val;
Xaa at position 22 is Asp, Leu, or Val;
Xaa at position 23 is Phe, Ser, Pro, Trp, or Ile;
Xaa at position 24 is Asn, or Ala;
Xaa at position 26 is Leu, Trp, or Arg;
20 Xaa at position 27 is Asn, Cys, Arg, Leu, His, Met, Pro;
Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Lys, Asn,
Thr, Leu, Val, Glu, Phe, Tyr, Ile or Met;
Xaa at position 29 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
Cys, Gln, Arg, Thr, Gly or Ser;
25 Xaa at position 30 is Asp, Ser, Leu, Arg, Lys, Thr, Met,
Trp, Glu, Asn, Gln, Ala or Pro;
Xaa at position 31 is Gln, Pro, Phe, Val, Met, Leu, Thr,
Lys, Asp, Asn, Arg, Ser, Ala, Ile, Glu, His or Trp;
Xaa at position 32 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,
30 Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;
Xaa at position 33 is Ile, Gly, Val, Ser, Arg, Pro, or
His;
Xaa at position 34 is Leu, Ser, Cys, Arg, Ile, His, Phe,
Glu, Lys, Thr, Ala, Met, Val or Asn;

407

- Xaa at position 35 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;
- Xaa at position 36 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, Ala, Ile, Val, His, Phe, Met or Gln;
- 5 Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- Xaa at position 38 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
- Xaa at position 39 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, Met, or;
- 10 Xaa at position 40 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala or Leu;
- Xaa at position 41 is Arg, Thr, Val, Ser, Leu, or Gly;
- Xaa at position 42 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
- 15 Xaa at position 43 is Asn or Gly;
- Xaa at position 44 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;
- Xaa at position 45 is Glu Tyr, His, Leu, Pro, or Arg;
- 20 Xaa at position 46 is Ala, Ser, Pro, Tyr, Asn, or Thr;
- Xaa at position 47 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
- Xaa at position 48 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;
- 25 Xaa at position 49 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val;
- Xaa at position 50 is Ala, Asn, Pro, Ser, or Lys;
- Xaa at position 51 is Val, Thr, Pro, His, Leu, Phe, or Ser;
- 30 Xaa at position 52 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;
- Xaa at position 53 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His;
- Xaa at position 54 is Leu, Val, Trp, Ser, Ile, Phe, Thr,

- or His;
- Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or Leu;
- Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala;
- 5 Xaa at position 57 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, Trp, or Asn;
- Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;
- Xaa at position 59 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;
- 10 Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu;
- Xaa at position 62 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;
- 15 Xaa at position 63 is Ile, Ser, Arg, Thr, or Leu;
- Xaa at position 64 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile, or Asp;
- 20 Xaa at position 66 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or Arg;
- Xaa at position 67 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or Lys;
- 25 Xaa at position 68 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
- Xaa at position 69 is Pro, Ala, Thr, Trp, Arg, or Met;
- Xaa at position 70 is Cys, Glu, Gly, Arg, Met, or Val;
- Xaa at position 71 is Leu, Asn, Val, or Gln;
- 30 Xaa at position 72 is Pro, Cys, Arg, Ala, or Lys;
- Xaa at position 73 is Leu, Ser, Trp, or Gly;
- Xaa at position 74 is Ala, Lys, Arg, Val, or Trp;
- Xaa at position 75 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, or Ser;

- Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
or Met;
- Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
or His;
- 5 Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala,
Gly, Ile or Leu;
- Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;
- Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln,
10 Lys, His, Ala or Pro;
- Xaa at position 81 is His, Gln, Pro, Arg, Val, Leu, Gly,
Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile or Tyr;
- Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- Xaa at position 83 is Ile, Val, Lys, Ala, or Asn;
- 15 Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr,
Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- Xaa at position 85 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
Gly, Ser, Phe, or His;
- Xaa at position 86 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
20 Gln, Pro;
- Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu or Gln;
- Xaa at position 88 is Gly, Leu, Glu, Lys, Ser, Tyr, or
Pro;
- 25 Xaa at position 89 is Asp, or Ser;
- Xaa at position 90 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
Leu, Gln, Lys, Ala, Phe, or Gly;
- Xaa at position 91 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
Tyr, Leu, Lys, Ile, Asp, or His;
- 30 Xaa at position 92 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
or Pro;
- Xaa at position 94 is Arg, Lys, Asp, Leu, Thr, Ile, Gln,
His, Ser, Ala, or Pro;
- Xaa at position 95 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,

410

- or Gly;
- Xaa at position 96 is Lys, Asn, Thr, Leu, Gln, Arg,
His, Glu, Ser, Ala or Trp;
- Xaa at position 97 is Leu, Ile, Arg, Asp, or Met;
- 5 Xaa at position 98 is Thr, Val, Gln, Tyr, Glu, His, Ser,
or Phe;
- Xaa at position 99 is Phe, Ser, Cys, His, Gly, Trp, Tyr,
Asp, Lys, Leu, Ile, Val or Asn;
- Xaa at position 100 is Tyr, Cys, His, Ser, Trp, Arg, or
10 Leu;
- Xaa at position 101 is Leu, Asn, Val, Pro, Arg, Ala, His,
Thr, Trp, or Met;
- Xaa at position 102 is Lys, Leu, Pro, Thr, Met, Asp, Val,
Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or
15 Ile;
- Xaa at position 103 is Thr, Ser, Asn, Ile, Trp, Lys, or
Pro;
- Xaa at position 104 is Leu, Ser, Pro, Ala, Glu, Cys, Asp,
or Tyr;
- 20 Xaa at position 105 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr,
or Arg;
- Xaa at position 106 is Asn, Ala, Pro, Leu, His, Val, or
Gln;
- Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Lys, Asp,
25 or Gly;
- Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;
- Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr,
or Leu;
- 30

and which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding native amino acids of (1-133) human

411

interleukin-3;

R2 is a colony stimulating factor; and

L is a linker capable of Linking R1 to R2.

5

7. The fusion protein of claim 6 wherein said colony stimulating factor is selected from the group consisting of GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF)

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8. The fusion protein of claim 7 wherein R1 is of the Formula:

20 Asn Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Xaa Leu Lys Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa
20 25 30

25 Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu
35 40 45

30 Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile
50 55 60

Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr
65 70 75

35 Ala Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa

412

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Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:5]

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wherein

Xaa at position 3 is Ser, Gly, Asp, Met, or Gln;

Xaa at position 4 is Asn, His, or Ile;

Xaa at position 5 is Met or Ile;

Xaa at position 7 is Asp or Glu;

19

Xaa at position 9 is Ile, Ala, Leu, or Gly;

Xaa at position 10 is Ile, Val, or Leu;

Xaa at position 11 is Thr, His, Gln, or Ala;

Xaa at position 12 is His or Ala;

Xaa at position 15 is Gln, Asn, or Val;

20

Xaa at position 16 is Pro, Gly, or Gln;

Xaa at position 17 is Pro, Asp, Gly, or Gln;

Xaa at position 18 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu;

Xaa at position 19 is Pro or Glu;

25

Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Ala, Arg,
Gln, Glu, Ile, Phe, Thr or Met;

Xaa at position 21 is Leu, Ala, Asn, Pro, Gln, or Val;

Xaa at position 23 is Phe, Ser, Pro, or Trp;

Xaa at position 24 is Asn or Ala;

30

Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Asn, Ile,
Leu, Met Tyr or Arg;

Xaa at position 30 is Asp or Glu;

Xaa at position 31 is Gln, Val, Met, Leu, Thr, Ala, Asn,
Glu, Ser or Lys;

- Xaa at position 32 is Asp, Phe, Ser, Thr, Ala, Asn, Gln,
Glu, His, Ile, Lys, Tyr, Val or Cys;
- Xaa at position 36 is Glu, Ala, Asn, Ser or Asp;
- Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or
5 His;
- Xaa at position 40 is Arg or Ala;
- Xaa at position 41 is Arg, Thr, Val, Leu, or Gly;
- Xaa at position 42 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
Glu, Leu, Thr, Val Or Lys;
- 10 Xaa at position 46 is Ala or Ser;
- Xaa at position 48 is Asn, Pro, Thr, or Ile;
- Xaa at position 49 is Arg or Lys;
- Xaa at position 50 is Ala or Asn;
- Xaa at position 51 is Val or Thr;
- 15 Xaa at position 52 is Lys or Arg;
- Xaa at position 53 is Ser, Phe, or His;
- Xaa at position 54 is Leu, Ile, Phe, or His;
- Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, or
Gly;
- 20 Xaa at position 57 is Ala, Pro, or Arg;
- Xaa at position 58 is Ser, Glu, Arg, or Asp;
- Xaa at position 59 is Ala or Leu;
- Xaa at position 62 is Ser, Val, Ala, Asn, Glu, Pro, or
Gly;
- 25 Xaa at position 63 is Ile or Leu;
- Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
Gly, or Asp;
- Xaa at position 66 is Asn, Gly, Glu, or Arg;
- Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
30 Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
- Xaa at position 69 is Pro or Thr;
- Xaa at position 71 is Leu or Val;
- Xaa at position 73 is Leu or Ser;
- Xaa at position 74 is Ala or Trp;

- Xaa at position 77 is Ala or Pro;
- Xaa at position 79 is Thr, Asp, Ser, Pro, Ala, Leu, or Arg;
- Xaa at position 81 is His, Pro, Arg, Val, Leu, Gly, Asn,
- 5 Phe, Ser or Thr;
- Xaa at position 82 is Pro or Tyr;
- Xaa at position 83 is Ile or Val;
- Xaa at position 84 is His, Ile, Asn, Leu, Ala, Thr, Leu, Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;
- 10 Xaa at position 85 is Ile, Leu, or Val;
- Xaa at position 86 is Lys, Arg, Ile, Gln, Pro, or Ser;
- Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Asn, Ile, Leu or Tyr;
- Xaa at position 90 is Trp or Leu;
- 15 Xaa at position 91 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr, Leu, Lys, Ile, Asp, or His;
- Xaa at position 92 is Glu, or Gly;
- Xaa at position 94 is Arg, Ala, or Ser;
- Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
- 20 Xaa at position 98 is Thr, Val, or Gln;
- Xaa at position 100 is Tyr or Trp;
- Xaa at position 101 is Leu or Ala;
- Xaa at position 102 is Lys, Thr, Val, Trp, Ser, Ala, His, Met, Phe, Tyr or Ile;
- 25 Xaa at position 103 is Thr or Ser;
- Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
- Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Asp, or Gly;
- Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
- 30 His, Ile, Tyr, or Cys;
- Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;

which can additionally have Met- or Met-Ala- preceding the

415

amino acid in position 1; and wherein from 4 to 35 of the amino acids designated by Xaa are different from the corresponding amino acids of native human interleukin-3.

5 9. The fusion protein of claim 8 wherein R₁ is of the Formula:

| | | | | |
|----|---|-----|-----|-----|
| 10 | 1 | 5 | 10 | 15 |
| | Asn Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa | | | |
| | Xaa Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp | 20 | 25 | 30 |
| 15 | Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu | 35 | 40 | 45 |
| | Ala Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile | 50 | 55 | 60 |
| 20 | Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr | 65 | 70 | 75 |
| | Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Xaa Gly Asp Trp | 80 | 85 | 90 |
| 25 | Xaa Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu | 95 | 100 | 105 |
| 30 | Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:6] | 110 | | |

wherein

Xaa at position 3 is Ser, Gly, Asp, or Gln;

Xaa at position 4 is Asn, His, or Ile;

35 Xaa at position 9 is Ile, Ala, Leu, or Gly;

- Xaa at position 11 is Thr, His, or Gln;
Xaa at position 12 is His or Ala;
Xaa at position 15 is Gln or Asn;
Xaa at position 16 is Pro or Gly;
5 Xaa at position 18 is Leu, Arg, Asn, or Ala;
Xaa at position 20 is Leu, Val, Ser, Ala, Arg, Gln, Glu,
Ile, Phe, Thr or Met;
Xaa at position 21 is Leu, Ala, Asn, or Pro;
Xaa at position 24 is Asn or Ala;
10 Xaa at position 28 is Gly, Asp, Ser, Ala, Asn, Ile, Leu,
Met, Tyr or Arg;
Xaa at position 31 is Gln, Val, Met, Leu, Ala, Asn, Glu or
Lys;
Xaa at position 32 is Asp, Phe, Ser, Ala, Gln, Glu, His,
15 Val or Thr;
Xaa at position 36 is Glu, Asn, Ser or Asp;
Xaa at position 37 is Asn, Arg, Pro, Thr, or His;
Xaa at position 41 is Arg, Leu, or Gly;
Xaa at position 42 is Pro, Gly, Ser, Ala, Asn, Val, Leu or
20 Gln;
Xaa at position 48 is Asn, Pro, or Thr;
Xaa at position 50 is Ala or Asn;
Xaa at position 51 is Val or Thr;
Xaa at position 53 is Ser or Phe;
25 Xaa at position 54 is Leu or Phe;
Xaa at position 55 is Gln, Ala, Glu, or Arg;
Xaa at position 62 is Ser, Val, Asn, Pro, or Gly;
Xaa at position 63 is Ile or Leu;
Xaa at position 65 is Lys, Asn, Met, Arg, Ile, or Gly;
30 Xaa at position 66 is Asn, Gly, Glu, or Arg;
Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
His, Met, Phe, Ser, Thr, Tyr or Val;
Xaa at position 73 is Leu or Ser;
Xaa at position 74 is Ala or Trp;

417

- Xaa at position 77 is Ala or Pro;
Xaa at position 79 is Thr, Asp, or Ala;
Xaa at position 81 is His, Pro, Arg, Val, Gly, Asn, Ser or Thr;
5 Xaa at position 84 is His, Ile, Asn, Ala, Thr, Arg, Gln, Glu, Lys, Met, Ser, Tyr, Val or Leu;
Xaa at position 85 is Ile or Leu;
Xaa at position 86 is Lys or Arg;
Xaa at position 87 is Asp, Pro, Met, Lys, His, Pro, Asn,
10 Ile, Leu or Tyr;
Xaa at position 91 is Asn, Pro, Ser, Ile or Asp;
Xaa at position 94 is Arg, Ala, or Ser;
Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
Xaa at position 98 is Thr or Gln;
15 Xaa at position 102 is Lys, Val, Trp, or Ile;
Xaa at position 103 is Thr, Ala, His, Phe, Tyr or Ser;
Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
Xaa at position 107 is Ala, Ser, Ile, Pro, or Asp;
Xaa at position 108 is Gln, Met, Trp, Phe, Pro, His, Ile,
20 or Tyr;
Xaa at position 109 is Ala, Met, Glu, Ser, or Leu;

and which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 26 of
25 the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133)human interleukin-3.

10. The fusion protein of claim 9 wherein R1
30 is of the Formula:

Xaa at position 17 is Ser, Lys, Asp, Met, Gln, or Arg;
Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or
35 Gln;

418

- Xaa at position 19 is Met, Arg, Gly, Ala, or Cys;
Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or
Ala;
Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, or
5 Val;
Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, or
Gly;
Xaa at position 23 is Ile, Ala, Gly, Trp, Lys, Leu, Ser,
or Arg;
10 Xaa at position 24 is Ile, Gly, Arg, or Ser;
Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or
Ala;
Xaa at position 26 is His, Thr, Phe, Gly, Ala, or Trp;
Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
15 Xaa at position 28 is Lys, Leu, Gln, Gly, Pro, Val or Trp;
Xaa at position 29 is Gln, Asn, Pro, Arg, or Val;
Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser,
Leu, or Lys;
Xaa at position 31 is Pro, Asp, Gly, Arg, Leu, or Gln;
20 Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or
Glu;
Xaa at position 33 is Pro, Leu, Gln, Thr, or Glu;
Xaa at position 34 is Leu, Gly, Ser, or Lys;
Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, or Gln;
25 Xaa at position 36 is Asp, Leu, or Val;
Xaa at position 37 is Phe, Ser, or Pro;
Xaa at position 38 is Asn, or Ala;
Xaa at position 40 is Leu, Trp, or Arg;
Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, Pro;
30 Xaa at position 42 is Gly, Asp, Ser, Cys, or Ala;
Xaa at position 42 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
Cys, or Ser;
Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met,
Trp, or Pro;

- Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr,
Lys, or Trp;
- Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, or Gly;
- Xaa at position 47 is Ile, Gly, Ser, Arg, Pro, or His;
- 5 Xaa at position 48 is Leu, Ser, Cys, Arg, His, Phe, or
Asn;
- Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
or Asp;
- Xaa at position 50 is Glu, Leu, Thr, Asp, or Tyr;
- 10 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
His;
- Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or
Thr;
- Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys,
15 Ser, or;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
or Leu;
- Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, or Lys;
- 20 Xaa at position 57 is Asn or Gly;
- Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or
Cys;
- Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;
- Xaa at position 60 is Ala, Ser, Tyr, Asn, or Thr;
- 25 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or
Ser;
- Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, or Ile;
- Xaa at position 63 is Arg, Tyr, Trp, Ser, Pro, or Val;
- Xaa at position 64 is Ala, Asn, Ser, or Lys;
- 30 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or
Ser;
- Xaa at position 66 is Lys, Ile, Val, Asn, Glu, or Ser;
- Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile,
Pro, or His;

420

- Xaa at position 68 is Leu, Val, Trp, Ser, Thr, or His;
Xaa at position 69 is Gln, Ala, Pro, Thr, Arg, Trp, Gly,
or Leu;
Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
5 Xaa at position 71 is Ala, Met, Leu, Arg, Glu, Thr, Gln,
Trp, or Asn;
Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg,
or Asp;
Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr,
10 or Arg;
Xaa at position 74 is Ile, Thr, Pro, Arg, Gly, Ala;
Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg,
Ser, or Leu;
Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro,
15 Gly, or Asp;
Xaa at position 77 is Ile, Ser, Arg, or Thr;
Xaa at position 78 is Leu, Ala, Ser, Glu, Gly, or Arg;
Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Ile, or
Asp;
20 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, or
Arg;
Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, or
Lys;
Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, or Asp;
25 Xaa at position 83 is Pro, Thr, Trp, Arg, or Met;
Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
Xaa at position 85 is Leu, Asn, or Gln;
Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
Xaa at position 87 is Leu, Ser, Trp, or Gly;
30 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,
or Asn;
Xaa at position 90 is Ala, Ser, Asp, Ile, or Met;
Xaa at position 91 is Ala, Ser, Thr, Phe, Leu, Asp, or

421

- His;
- Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, or Leu;
- 5 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;
- Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, or Pro;
- Xaa at position 95 is His, Gln, Pro, Val, Leu, Thr or Tyr;
- Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- 10 Xaa at position 97 is Ile, Lys, Ala, or Asn;
- Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, or Pro;
- Xaa at position 99 is Ile, Arg, Asp, Pro, Gln, Gly, Phe, or His;
- 15 Xaa at position 100 is Lys, Tyr, Leu, His, Ile, Ser, Gln, or Pro;
- Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val, Tyr, or Gln;
- Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- 20 Xaa at position 103 is Asp, or Ser;
- Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, Gln, Lys, Ala, Phe, or Gly;
- Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr; Leu, Lys, Ile, or His;
- 25 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;
- Xaa at position 108 is Arg, Asp, Leu, Thr, Ile, or Pro;
- Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly.
- 30

11. The fusion protein of claim 10 wherein R₁ is of the Formula:

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422

1 5 10
 (Met)_m-Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr
 15 20
 Ser Trp Val Asn Cys Ser Xaa Xaa Xaa Asp Glu Ile Ile
 5 25 30 35
 Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa
 40 45 50
 Xaa Asn Leu Asn Xaa Glu Asp Xaa Asp Ile Leu Xaa Glu
 55 60
 10 Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa
 65 70 75
 Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa
 80 85
 Ile Leu Xaa Asn Leu Xaa Pro Cys Xaa Pro Xaa Xaa Thr
 15 90 95 100
 Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly
 105 110 115
 Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu
 120 125
 20 Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln Thr Thr Leu
 130
 Ser Leu Ala Ile Phe [SEQ ID NO:7]

wherein m is 0 or 1; Xaa at position 18 is Asn or Ile; Xaa
 25 at position 19 is Met, Ala or Ile; Xaa at position 20 is
 Ile, Pro or Ile; Xaa at position 23 is Ile, Ala or Leu; Xaa
 at position 25 is Thr or His; Xaa at position 29 is Gln,
 Arg, Val or Ile; Xaa at position 32 is Leu, Ala, Asn or Arg;
 Xaa at position 34 is Leu or Ser; Xaa at position 37 is Phe,
 30 Pro, or Ser; Xaa at position 38 is Asn or Ala; Xaa at
 position 42 is Gly, Ala, Ser, Asp or Asn; Xaa at position 45
 is Gln, Val, or Met; Xaa at position 46 is Asp or Ser; Xaa
 at position 49 is Met, Ile, Leu or Asp; Xaa at position 50
 is Glu or Asp; Xaa at position 51 is Asn Arg or Ser; Xaa at
 35 position 55 is Arg, Leu, or Thr; Xaa at position 56 is Pro

423

or Ser; Xaa at position 59 is Glu or Leu; Xaa at position 60 is Ala or Ser; Xaa at position 62 is Asn, Val or Pro; Xaa at position 63 is Arg or His; Xaa at position 65 is Val or Ser; Xaa at position 67 is Ser, Asn, His or Gln; Xaa at position 5 69 is Gln or Glu; Xaa at position 73 is Ala or Gly; Xaa at position 76 is Ser, Ala or Pro; Xaa at position 79 is Lys, Arg or Ser; Xaa at position 82 is Leu, Glu, Val or Trp; Xaa at position 85 is Leu or Val; Xaa at position 87 is Leu, Ser, Tyr; Xaa at position 88 is Ala or Trp; Xaa at position 10 91 is Ala or Pro; Xaa at position 93 is Pro or Ser; Xaa at position 95 is His or Thr; Xaa at position 98 is His, Ile, or Thr; Xaa at position 100 is Lys or Arg; Xaa at position 101 is Asp, Ala or Met; Xaa at position 105 is Asn or Glu; Xaa at position 109 is Arg, Glu or Leu; Xaa at position 112 15 is Thr or Gln; Xaa at position 116 is Lys, Val, Trp or Ser; Xaa at position 117 is Thr or Ser; Xaa at position 120 is Asn, Gln, or His; Xaa at position 123 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino 20 acids of native human interleukin-3.

12. The fusion protein of claim 11 wherein R₁ is of the Formula:

| | | | |
|----|--|-------------------------|-------------|
| 25 | 1 | 5 | 10 |
| | (Met ^m -Alan) _p -Asn | Cys Ser Xaa Xaa Xaa Asp | Glu Xaa Ile |
| | 15 | 20 | |
| | Xaa His Leu Lys Xaa Pro | Pro Xaa Pro Xaa Leu Asp | Xaa |
| 30 | 25 | 30 | 35 |
| | Xaa Asn Leu Asn Xaa Glu Asp | Xaa Xaa Ile Leu Xaa Glu | |
| | 40 | 45 | |
| | Xaa Asn Leu Arg Xaa Xaa Asn Leu | Xaa Xaa Phe Xaa Xaa | |
| | 50 | 55 | 60 |
| 35 | Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser | Xaa Ile Glu Xaa | |

424

65 70 75
 Ile Leu Xaa Asn Xaa Xaa Pro Cys Xaa Pro Xaa Ala Thr
 80 85
 Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly
 5 90 95 100
 Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu
 105 110
 Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln [SEQ ID NO:8]

- 10 wherein m is 0 or 1; n is 0 or 1; p is 0 or 1; Xaa at position 4 is Asn or Ile; Xaa at position 5 is Met, Ala or Ile; Xaa at position 6 is Ile, Pro or Leu; Xaa at position 9 is Ile, Ala or Leu; Xaa at position 11 is Thr or His; Xaa at position 15 is Gln, Arg, Val or Ile; Xaa at position 18 is
- 15 Leu, Ala, Asn or Arg; Xaa at position 20 is Leu or Ser; Xaa at position 23 is Phe, Pro, or Ser; Xaa at position 24 is Asn or Ala; Xaa at position 28 is Gly, Ala, Ser, Asp or Asn; Xaa at position 31 is Gln, Val, or Met; Xaa at position 32 is Asp or Ser; Xaa at position 35 is Met, Ile or Asp; Xaa at
- 20 position 36 is Glu or Asp; Xaa at position 37 is Asn, Arg or Ser; Xaa at position 41 is Arg, Leu, or Thr; Xaa at position 42 is Pro or Ser; Xaa at position 45 is Glu or Leu; Xaa at position 46 is Ala or Ser; Xaa at position 48 is Asn, Val or Pro; Xaa at position 49 is Arg or His; Xaa at position 51 is
- 25 Val or Ser; Xaa at position 53 is Ser, Asn, His or Gln; Xaa at position 55 is Gln or Glu; Xaa at position 59 is Ala or Gly; Xaa at position 62 is Ser, Ala or Pro; Xaa at position 65 is Lys, Arg or Ser; Xaa at position 67 is Leu, Glu, or Val; Xaa at position 68 is Leu, Glu, Val or Trp; Xaa at
- 30 position 71 is Leu or Val; Xaa at position 73 is Leu, Ser or Tyr; Xaa at position 74 is Ala or Trp; Xaa at position 77 is Ala or Pro; Xaa at position 79 is Pro or Ser; Xaa at position 81 is His or Thr; Xaa at position 84 is His, Ile, or Thr; Xaa at position 86 is Lys or Arg; Xaa at position 87

425

is Asp, Ala or Met; Xaa at position 91 is Asn or Glu; Xaa at position 95 is Arg, Glu, Leu; Xaa at position 98 Thr or Gln; Xaa at position 102 is Lys, Val, Trp or Ser; Xaa at position 103 is Thr or Ser; Xaa at position 106 is Asn, Gln, or His; Xaa at position 109 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native (15-125)human interleukin-3.

10 13. The fusion protein of claim 12 wherein R₁ is of the Formula:

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
15 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
20 Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:9];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
25 Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
30 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:10];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
35 Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser

426

Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:11];

5

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
10 Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:12];

15

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
20 Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:13];

25

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
30 Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:14];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly

427

Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
5 Asp Trp Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:15];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
10 Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
15 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:16];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
20 Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:17];

25 Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
30 Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:18];

428

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
5 Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:19];

10 Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
15 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:20];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
20 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
25 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:21];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
30 Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr

Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:22];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
5 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
10 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:23];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
15 Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:24];
20

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
25 Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:25];

30 Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser

430

Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:26];

5 Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
10 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:27];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
15 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
20 Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:28];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
25 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
30 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:29];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn

431

Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
5 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:30];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
10 Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:31];

15 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
20 Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:32];

25 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
30 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:33];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
5 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:34];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
10 Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
15 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:35];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
20 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
25 Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:36];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
30 Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:37];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
5 Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:38];
10
Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
15 Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:39].
20
Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Ser Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
25 Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:40]
30
Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ala Ile His His Leu
Lys Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
35 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:41]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
5 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
10 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:42]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
15 Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
20 Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:43]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
25 Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
30 Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:44]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp

435

Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
5 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:45]

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn
Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
10 Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val
Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu
Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
15 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln
Ala Gln Glu Gln Gln
[SEQ ID NO:46]

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn
Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu
25 Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln
Ala Gln Glu Gln Gln
[SEQ ID NO:47] and

30

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Leu Ile His His Leu
Lys Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu Asn Ser
Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser

436

Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:48].

5

14. The fusion protein of claim 13, wherein R₁
is of the Formula:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
10 Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
15 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:30].

15. The fusion protein of claims
1,2,3,4,5,6,7,8,9,10,11,12, 13, or 14 wherein said colony
20 stimulating factor is G-CSF or GM-CSF.

16 The fusion protein of claim 1 selected from
group consisting of amino acid sequences corresponding to
SEQ. ID. NO: 121-159 and 165-168.

25

17. The fusion protein of claim 1 selected from
group consisting of amino acid sequences corresponding to
SEQ. ID. NO: 133,124,154 and 155.

30

18. A pharmaceutical composition comprising a
therapeutically effective amount of the fusion protein of
claims 1,2,3,4,5,6,7,8,9,10,11,12,13,14,16 or 17 and a
pharmaceutically acceptable carrier.

19. A pharmaceutical composition comprising a therapeutically effective amount of the fusion protein of claim 15 and a pharmaceutically acceptable carrier.

5

20. A method of increasing hematopoietic cell production in a mammal in need thereof comprising administering a pharmaceutically effective amount of the fusion protein of claims 1,2,3,4,5,6,7,8,9,10,11,12,13,14,16
10 or 17.

21. A method of increasing hematopoietic cell production in a mammal in need thereof comprising administering a pharmaceutically effective amount of the
15 fusion protein of claim 15.

22. Recombinant DNA comprising vector DNA and DNA that encodes for a polypeptide selected from group consisting of nucleotide sequences corresponding to SEQ. ID.
20 NO: 53-90 and 183-186.

23. A recombinant DNA of claim 22 selected from group consisting of nucleotide sequences corresponding to SEQ. ID. NO: 60,64,89 and 98,
25

1/5

1 5 10
ATG GCT CCA ATG ACT CAG ACT ACT TCT CTT AAG ACT TCT
Met Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser

15 20 25
TGG GTT AAC TGC TCT AAC ATG ATC GAT GAA ATT ATA ACA
Trp Val Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr

30 35
CAC TTA AAG CAG CCA CCT TTG CCT TTG CTG GAC TTC AAC
His Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn

40 45 50
AAC CTC AAT GGG GAA GAC CAA GAC ATT CTG ATG GAA AAT
Asn Leu Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn

55 60
AAC CTT CGA AGG CCA AAC CTG GAG GCA TTC AAC AGG GCT
Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala

65 70 75
GTC AAG AGT TTA CAG AAT GCA TCA GCA ATT GAG AGC ATT
Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile

80 85 90
CTT AAA AAT CTC CTG CCA TGT CTG CCC CTG GCC ACG GCC
Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala

95 100
GCA CCC ACG CGA CAT CCA ATC CAT ATC AAG GAC GGT GAC
Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp

105 110 115
TGG AAT GAA TTC CGT CGT AAA CTG ACC TTC TAT CTG AAA
Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys

120 125
ACC TTG GAG AAC GCG CAG GCT CAA CAG ACC ACT CTG TCG
Thr Leu Glu Asn Ala Gln Ala Gln Gln Thr Thr Leu Ser

130
CTA GCG ATC TTT TAA TAA [SEQ ID NO:144]
Leu Ala Ile Phe END END [SEQ ID NO:128]

2/5

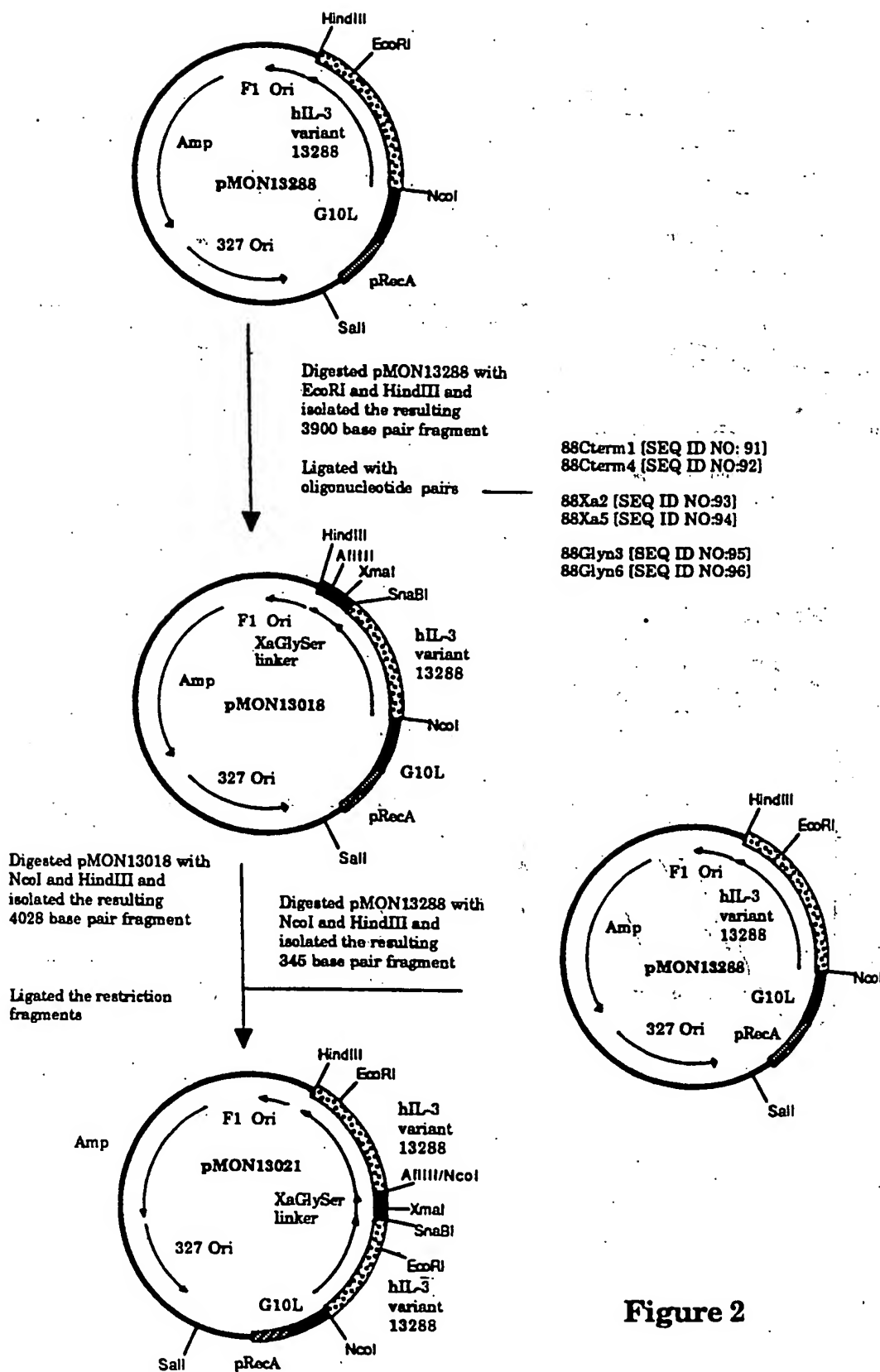


Figure 2

3/5

Figure 3

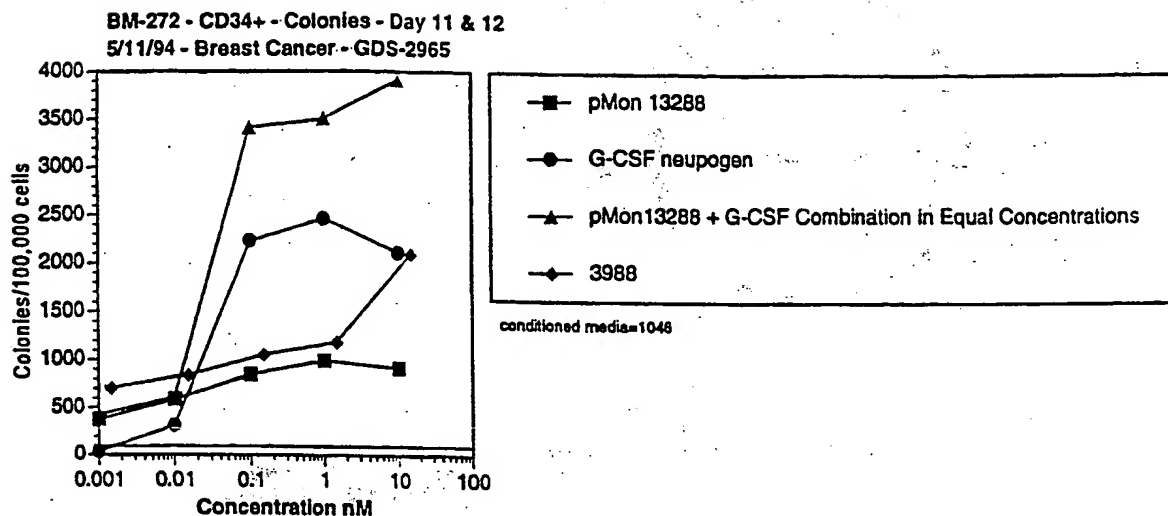


Figure 4

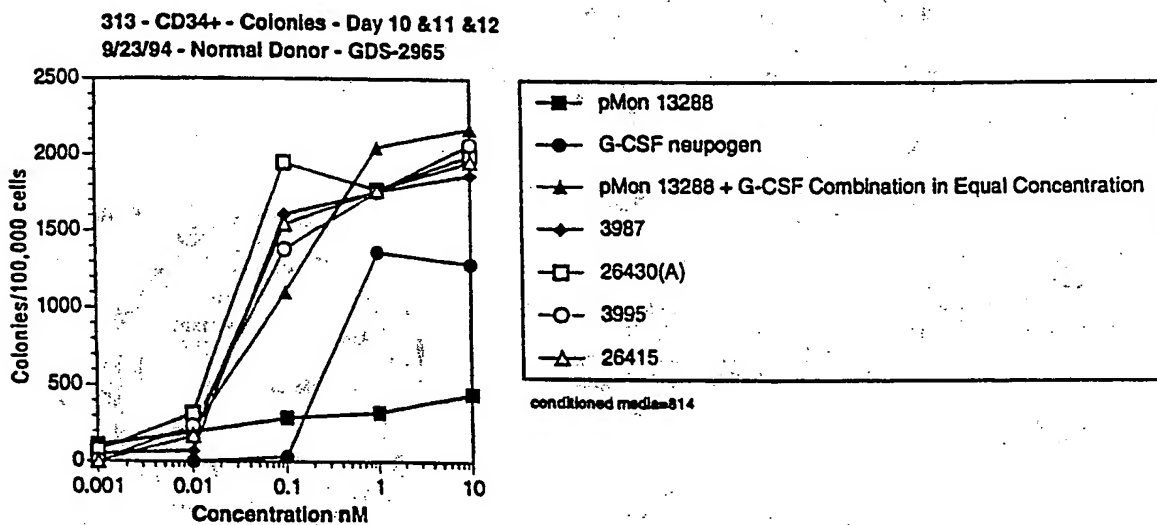


Figure 5

4/5

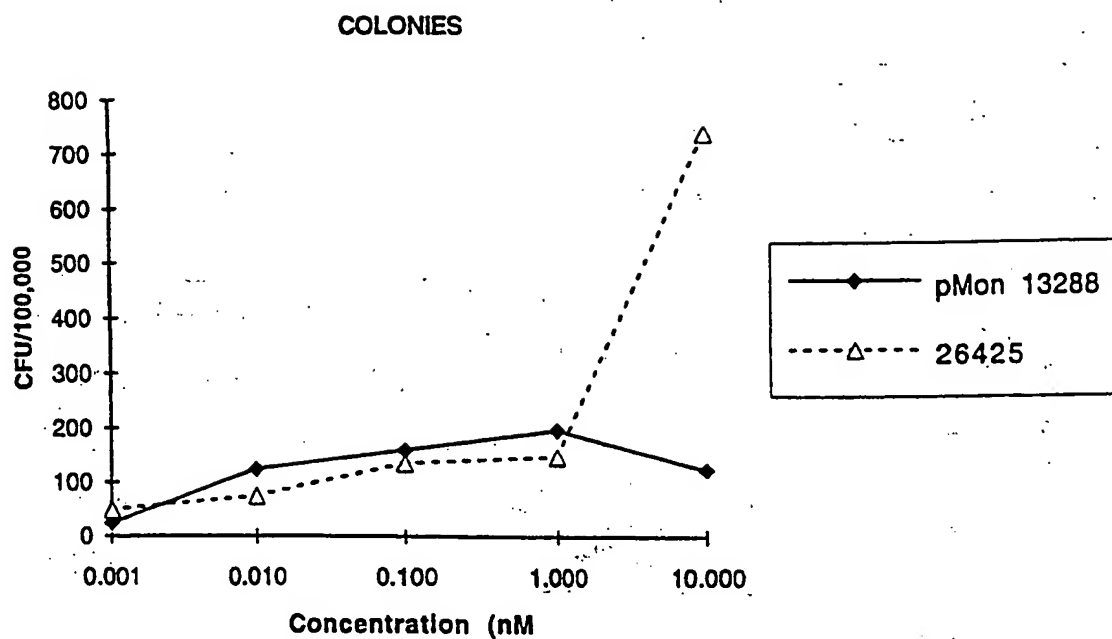
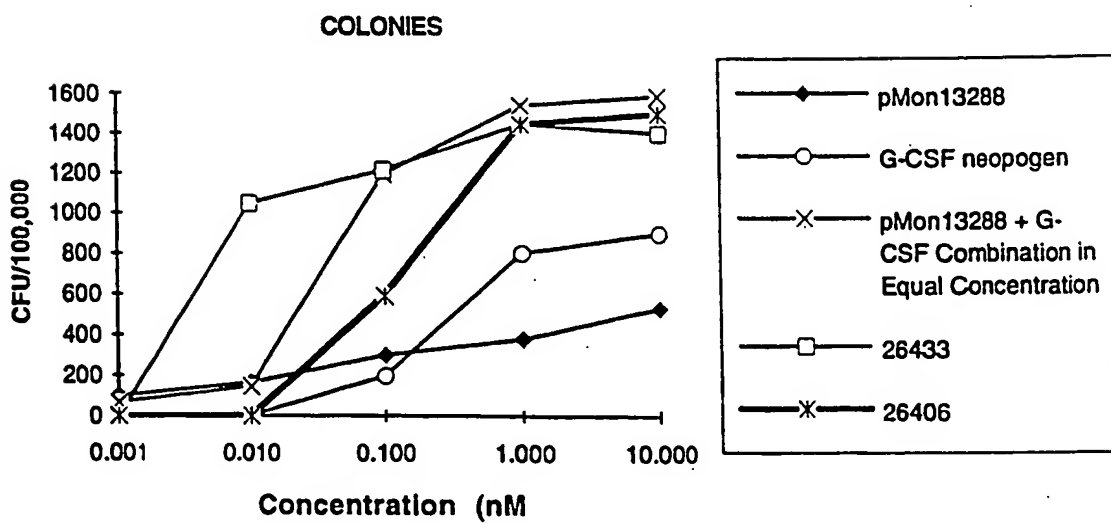
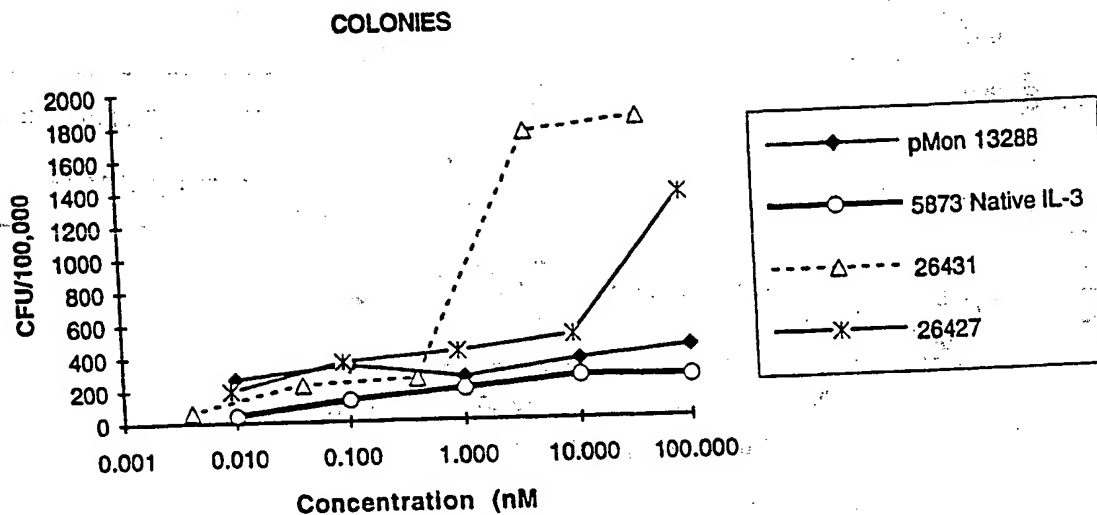


Figure 6



5/5

Figure 7



INTERNATIONAL SEARCH REPORT

International Application No
PC1/US 95/01185

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/24 C07K19/00 C07K14/54 A61K38/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| Y | WO,A,91 02754 (IMMUNEX CORPORATION) 7
March 1991
cited in the application
see the whole document
--- | 1-23 |
| Y | WO,A,92 06116 (ORTHO PHARMACEUTICAL
CORPORATION) 16 April 1992
see the whole document
--- | 1-23 |
| Y | WO,A,92 04455 (GENETICS INSTITUTE) 19
March 1992
cited in the application
see the whole document
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| P,Y | WO,A,94 12638 (SEARLE) 9 June 1994
see the whole document
----- | 1-23 |

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
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T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

2 June 1995

Date of mailing of the international search report

19-06-1995

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Fax (+31-70) 340-2040

Authorized officer

Moreau, J

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US95/01185

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark : Although claims 20-21 are directed to a method of treatment of the human/animal body the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 95/01185

| Patent document
cited in search report | Publication
date | Patent family
member(s) | Publication
date |
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